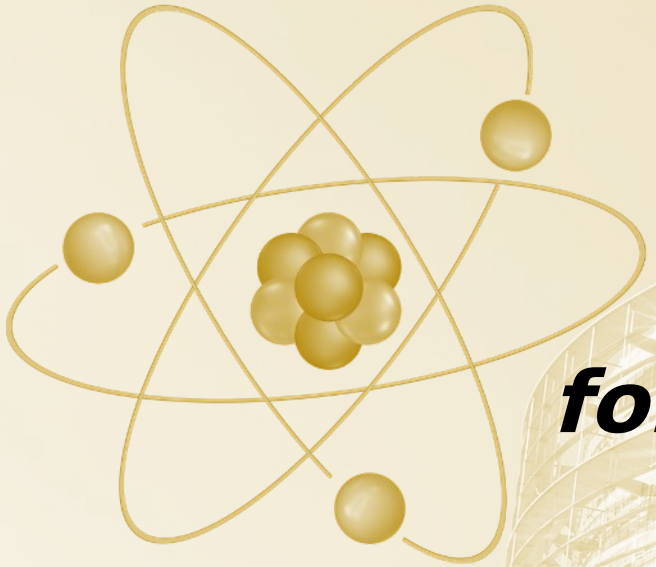
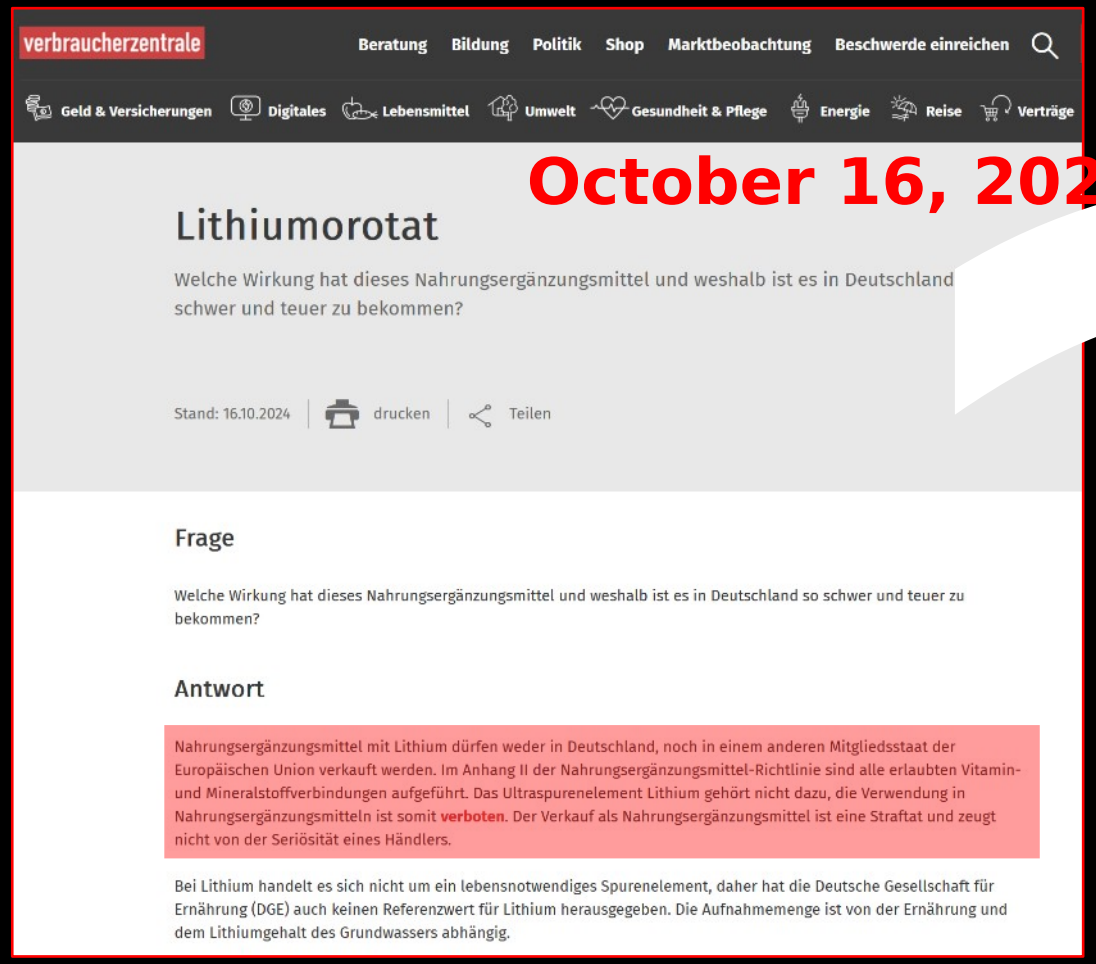


Essential lithium – the suppressed element for cognitive function, peace and democracy in Europe

European Parliament

Essentielles Lithium – das unterdrückte Element für Denk-, Friedens- und Demokratiefähigkeit in Europa

Michael Nehls, MD, PhD
EU-Parlament
June 18, 2025



October 16, 202

„Nahrungsergänzungsmittel mit Lithium dürfen weder in Deutschland, noch in einem n Mitgliedsstaat der Europäischen ion verkauft werden.“

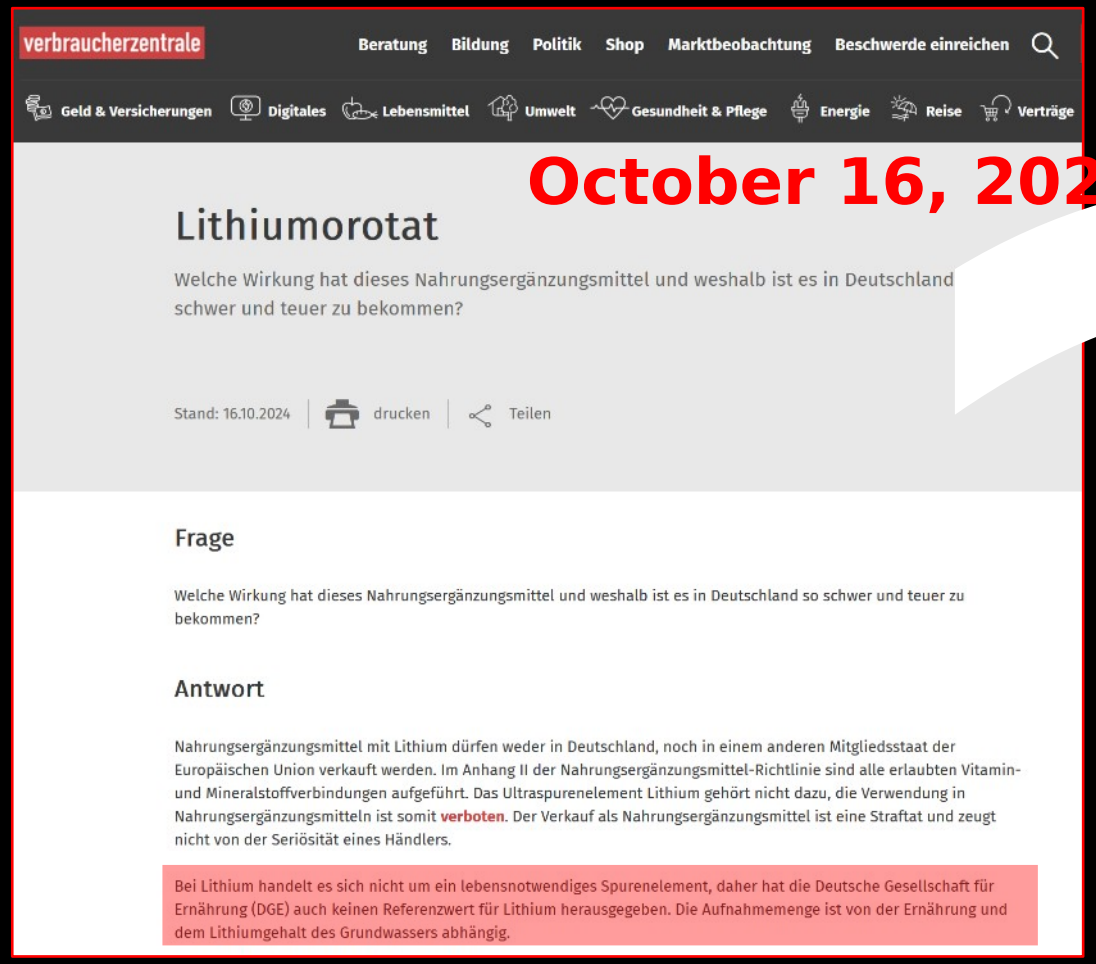
„Im An der Nahrungsergänzungsmittel-Richtl nd alle erlaubten Vitamin- und Miner verbindungen aufgeführt. Das Ultraspur ment Lithium gehört nicht dazu, die Verw g in Nahrungsergänzungsmitteln ist somit **verboten**.“

„D kauf als Nahrungsergänzungsmittel ist e **traftat** und zeugt nicht von der Seriösität eines Händlers.“

“Food supplements containing lithium m t be sold in Germany or any other European Union member state.”

“Annex II of the Food Supplements Directive lists all permitted vitamin and mineral compounds.’ As lithium is not include use in food supplements **is prohibited**.”

“Selling it as a food supplement constitu **criminal offence** and reflects poorly on the integrity of the retailer.”



October 16, 202

„Bei Lithium handelt es sich nicht um ein lebensnotwendiges Spurenelement, daher hat [illegible]che Gesellschaft für Ernährung (DGE) [illegible]inen Referenzwert für Lithium herausgegeben.“

„Die Aufn[illegible]menge ist von der Ernährung und dem Lithi[illegible]halt des Grundwassers abhängig.“

?

“Lithium is not an [illegible]ntial trace element, which is why the German Nutrition Society (DGE) has not issued a reference value for lithium.”

“The intake depends on diet a[illegible] lithium content of groundwater.”

s://www.verbraucherzentrale.de/faq/projekt-klartext-nem/lithiumorotat-40582

1996

Trace elements in human nutrition and health

World Health Organization
Geneva
1996

„Epidemiologische Studien in den USA haben einen inversen Zusammenhang zwischen Lithium im Trinkwasser und der Sterblichkeit, insbesondere aufgrund von Herzerkrankungen gezeigt [...].“

generations on severely lithium-deficient rations, but the survival of the litters and reproductive efficiency were significantly reduced. Tissue lithium concentrations were found to reflect dietary lithium supply, except in some endocrine and exocrine glands and areas of the brain, in which near-normal concentrations were maintained even after prolonged depletion (*8*).

Epidemiological studies in the USA have shown negative correlations between lithium in drinking-water and mortality, especially from heart disease (*9*), and admission rates to mental hospitals (*10*).

In summary lithium at high, near toxic doses effectively controls the symptoms of manic-depressive disorders. Toxicity from dietary lithium is unknown, the intake from dietary sources being approximately 100 μg/day or less and, typically, less than 0.1% of the therapeutic or potentially toxic doses. Lithium may have essential functions in experimental animals but it is not known whether there is a human requirement.

https://www.who.int/publications/i/item/

> Eur J Nutr. 2011 Aug;50(5):387-9. doi: 10.1007/s00394-011-0171-x. Epub 2011 Feb 8.

Low-dose lithium uptake promotes longevity in humans and metazoans

Kim Zarse [1], Takeshi Terao, Jing Tian, Noboru Iwata, Nobuyoshi Ishii, Michael Ristow

Affiliations – collapse

Affiliation

1 Department of Human Nutrition, Institute of Nutrition, University of Jena, Germany.

February 8, 2011

PMID: 21301855 PMCID: PMC3151375 DOI: 10.1007/s00394-011-0171-x

Conclusions: Taken together, these findings indicate that long-term low-dose exposure to lithium may exert anti-aging capabilities and unambiguously decreases mortality in evolutionary distinct species.

„Zusammengefasst deuten diese Ergebnisse darauf hin, dass eine langfristige Zufuhr niedriger Lithiumdosen Anti-Aging-Effekte aufweist und die Sterblichkeit bei evolutionär unterschiedlichen Arten [*Mensch, Nematode; aber auch Fruchtfliege oder Hefepilz*]

Observational Study > Appl Physiol Nutr Metab. 2018 Apr;43(4):412-414.

doi: 10.1139/apnm-2017-0653. Epub 2017 Dec 5.

Trace lithium in Texas tap water is negatively associated with all-cause mortality and premature death

Val Andrew Fajardo [1 2], Paul J LeBlanc [1 2], Val Andrei Fajardo [3]

Affiliations + expand

December 5, 2017

PMID: 29206474 DOI: 10.1139/apnm-2017-0653

Abstract

Lithium in tap water was previously found to have life-extending effects across 18 Japanese municipalities. Using a larger dataset with several Texas counties, our study shows that lithium concentrations in tap water are negatively associated with all-cause mortality (r = -0.18, p = 0.006, 232 counties) and years of potential life lost (r = -0.22, p = 0.001, 214 counties). Thus, our present findings extend and reinforce lithium's purported life-prolonging effect in humans.

„[…] Lithiumkonzentrationen im Leitungswasser stehen in einem negativen Zusammenhang mit der Gesamtsterblichkeit […] und den potenziell verlorenen Lebensjahren […]. Somit erweitern und bestätigen unsere aktuellen Ergebnisse die vermutete lebensverlängernde Wirkung von Lithium

JAMA Network Open

2025

Original Investigation | Environmental Health

Cancer Risk and Estimated Lithium Exposure in Drinking Groundwater in the US

Jiajun Luo, PhD, MPH; Liang Zheng, MD, PhD; Zhihao Jin, MPH; Yuqing Yang, MS; William Isaac Krakowka, MPH; Eric Hong, BS; Melissa Lombard, PhD; Joseph Ayotte, BS; Habibul Ahsan, MD; Jayant M. Pinto, MD; Briseis Aschebrook-Kilfoy, PhD, MPH

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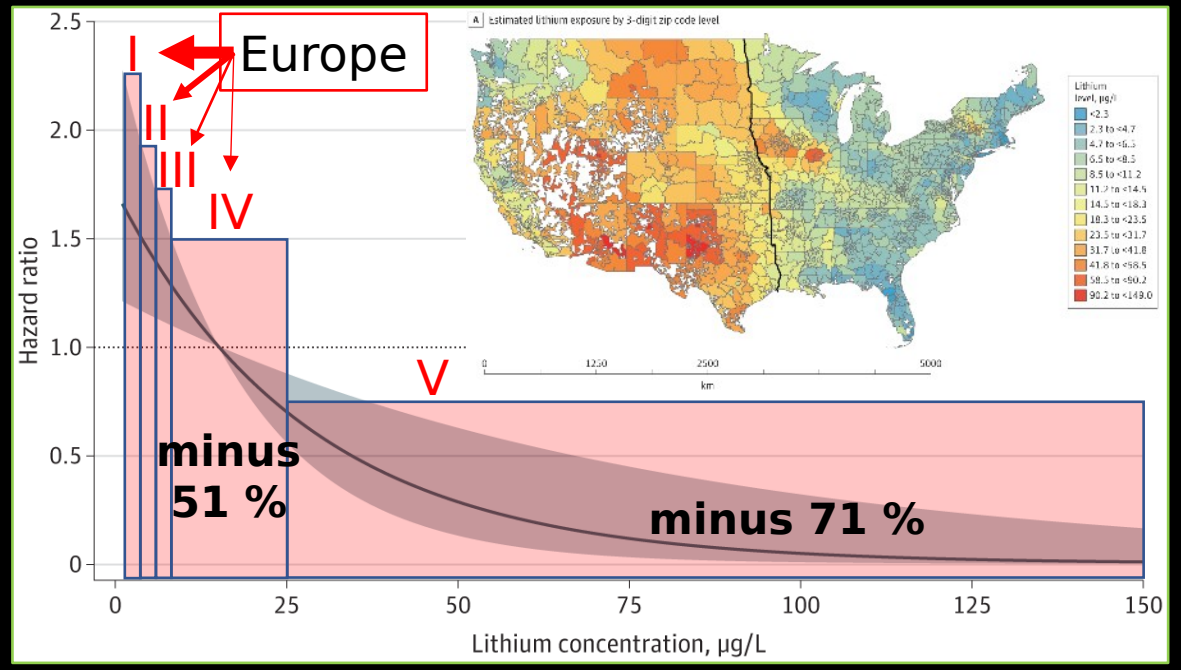
JAMA Network Open. 2025;8(2):e2460854. doi:10.1001/jamanetworkopen.2024.60854 February 20, 2025

Results A total of 252 178 participants were included (median age, 52 years [IQR, 36-64 years]; 60.1% female). The median follow-up time was 3.6 years (IQR, 3.0-4.3 years), and 7573 incident cancer cases were identified. Higher estimated lithium exposure was consistently associated with reduced cancer risk. Compared with the first (lowest) quintile of lithium exposure, the HR for all cancers was 0.49 (95% CI, 0.31-0.78) for the fourth quintile and 0.29 (95% CI, 0.15-0.55) for the fifth quintile. These associations were found for all cancer types investigated in both females and males, among long-term residents, and in both western and eastern states. For example, for the fifth vs first quintile of lithium exposure for all cancers, the HR was 0.17 (95% CI, 0.07-0.42) in females and 0.13 (95% CI, 0.04-0.38) in males; for long-term residents, the HR was 0.32 (95% CI, 0.15-0.66) in females and 0.24 (95% CI, 0.11-0.52) in males; and the HR was 0.01 (95% CI, 0.00-0.09) in western states and 0.34 (95% CI, 0.21-0.57) in eastern states.



https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2830452

„Diese Zusammenhänge wurden für alle untersuchten Krebsarten sowohl bei Frauen als auch bei Männern, bei Langzeitbewohnern sowie in westlichen und östlichen Bundesstaaten festgestellt.“

„Im Vergleich zum ersten (niedrigsten) Quintil der Lithiumexposition betrug das HR (Hazard Ratio) für alle Krebsarten **0,49** (95 % CI, 0,31–0,78) für das vierte Quintil und **0,29** (95 % CI, 0,15–0,55) für das fünfte Quintil.“

Introduction

Lithium is a naturally occurring element and can be commonly found in groundwater, particularly in arid areas in the western US, leading to widespread exposure through drinking water among the general population.[1] As lithium demonstrates mood-stabilizing effects,[2] it has been extensively used as a psychiatric medication for bipolar disorder, schizophrenia, and depression.[3-6] The toxic serum level for lithium is close to its therapeutic level.[7] Researchers have documented long-term adverse effects of lithium treatment on kidney and thyroid functions.[8,9] However, several observational studies among patients with bipolar disorder have reported an association between receiving lithium treatment and reduced cancer risk.[10-12] At the biological level, lithium has also been found to affect several enzymes that are implicated in cancer progression,[13] such as glycogen synthase kinase-3[14] and inositol monophosphate,[15] providing a plausible biological basis for potential anticancer effects.

Auf biologischer Ebene wurde außerdem festgestellt, dass Lithium mehrere Enzyme [Signalprozessoren] beeinflusst, die an der Krebsprogression beteiligt sind[13], wie beispielsweise Glykogensynthasekinase-3[14] **[GSK-3]** und Inositolmonophosphatase[15] **[IMPase]**. Dies stellt eine plausible biologische Grundlage für dessen potenzielle krebsbekämpfende Wirkungen

1996

Trace elements in human nutrition and health

> Eur J Nutr. 2011 Aug;50(5):387-9. doi: 10.1007/s00394-011-0171-x. Epub 2011 Feb 8.

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Zusammengefasst deuten diese Ergebnisse darauf hin, dass eine langfristige Zufuhr niedriger Lithiumdosen Anti-Aging-Effekte aufweist und die Sterblichkeit bei evolutionär unterschiedlichen Arten [*Mensch, Nematode; aber auch Fruchtfliegeoder Hefepilz*] eindeutig senkt.

World Health Organization
Geneva
1996

„Epidemiologische Studien in den USA haben einen inversen Zusammenhang zwischen Lithium im Trinkwasser und der Sterblichkeit, insbesondere aufgrund von Herzerkrankungen gezeigt […].“

„Lithium kann bei Versuchstieren essentielle Funktionen haben […].“

generations on severely lithium-deficient rations, but the survival of the litters and reproductive efficiency were significantly reduced. Tissue lithium concentrations were found to reflect dietary lithium supply, except in some endocrine and exocrine glands and areas of the brain, in which near-normal concentrations were maintained even after prolonged depletion (*8*).

Epidemiological studies in the USA have shown negative correlations between lithium in drinking-water and mortality, especially from heart disease (*9*), and admission rates to mental hospitals (*10*).

In summary lithium at high, near toxic doses effectively controls the symptoms of manic-depressive disorders. Toxicity from dietary lithium is unknown, the intake from dietary sources being approximately 100 μg/day or less and, typically, less than 0.1% of the therapeutic or potentially toxic doses. Lithium may have essential functions in experimental animals but it is not known whether there is a human requirement.

https://www.who.int/publications/i/item/

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0163-4984/92/3403-0299 $04.20

1992

Evidence for Dietary Essentiality of Lithium in the Rat†

EDWARD E. PICKETT* AND BOYD L. O'DELL

Department of Biochemistry, 117 Schweitzer Hall, University of Missouri, Columbia, MO 65211

Received December 9, 1991; Revised February 27, 1992; Accepted March 2, 1992

*„The overall conclusion that Li is essential for reproduction in the rat was supported at a **confidence level exceeding 99%**. […] The impairment of reproductive and lactational performance suggests that **Li is an essential element**.*

„Die allgemeine Schlussfolgerung, dass Lithium (Li) für die Fort-pflanzung bei Ratten unerlässlich ist, wurde mit einer **Konfidenz von über 99 %** bestätigt. […] Die Beeinträchtigung der Fortpflanzungs- und Laktationsleistung lässt darauf schließen, dass **Lithium ein essentielles Element ist**.

„Bei Ratten mit **Lithiummangel wurde abnormales Verhalten** beobachtet, **das nach einer Lithiumergänzung** wieder **verschwand**. […].

Zusammenfassend zeigen die Ergebnisse einer lebenslangen lithiumarmen Ernährung über mehr als 15 Generationen von Ziegen, dass Lithium für die Fauna und **somit auch für den Menschen essentiell** sein könnte."

Biomed Res Trace Elements 16(3) : 169-176, 2005

2005

Review Articles

Recent progress in exploring the essentiality of the ultratrace element lithium to the nutrition of animals and man

Manfred Anke, Winfried Arnhold, Ulrich Schäfer, Ralf Müller[1)]

Institute of Nutrition and Environment, Faculty of Biology and Pharmacy, Friedrich Schiller University Jena, D-07743 Jena, Germany ; [1)] Society of Ecology and Environmental Chemistry Ltd., Zittauer Str. 27, D-99091 Erfurt, Germany

Abstract

A lithium content below 1.7 mg/kg diet dry matter (DM) had a particular effect on the growth, reproduction performance, wellness and mortality of goats. The significant shift of the sex ratio of kids toward females, reduced monoaminooxidase activity in the liver, and increased creatine kinase activity (a stress indicator) are also interesting results. The normative lithium requirement of animals (goats, pigs) amounts to < 2.5 mg/kg diet DM, while that of adult humans might amount to < 200 μg/day.

Abnormal behavior was observed in lithium-deficient rats, and this disappeared after lithium supplementation. This assessment is interesting in so far as the MAO hypothesis is discussed as a biochemical mechanism of a lithium therapy in humans.

In brief, the results of lifelong lithium-poor nutrition over > 15 generations of goats show that lithium may be essential to the fauna, and thus, to humans as well [29, 30].

Proof of Essentiality!

1996

Trace elements in human nutrition and health

„Lithium kann bei Versuchstieren essentielle Funktionen haben, …

World Health Organization
Geneva
1996

„Epidemiologische Studien in den USA haben einen inversen Zusammenhang zwischen Lithium im Trinkwasser und der Sterblichkeit, insbesondere aufgrund von Herzerkrankungen gezeigt […].“

„[…]und der der Einweisungsrate in psychiatrische Kliniken gezeigt […].“

generations on severely lithium-deficient rations, but the survival of the litters and reproductive efficiency were significantly reduced. Tissue lithium concentrations were found to reflect dietary lithium supply, except in some endocrine and exocrine glands and areas of the brain, in which near-normal concentrations were maintained even after prolonged depletion (*8*).

Epidemiological studies in the USA have shown negative correlations between lithium in drinking-water and mortality, especially from heart disease (*9*), and admission rates to mental hospitals (*10*).

In summary lithium at high, near toxic doses effectively controls the symptoms of manic-depressive disorders. Toxicity from dietary lithium is unknown, the intake from dietary sources being approximately 100 μg/day or less and, typically, less than 0.1% of the therapeutic or potentially toxic doses. Lithium may have essential functions in experimental animals but it is not known whether there is a human requirement.

https://www.who.int/publications/i/item/

Dis Nerv Syst. 1970 Dec;31(12):811-20.

1970

The mathematical relationship of drinking water lithium and rainfall to mental hospital admission

E B Dawson, T D Moore, W J McGanity

PMID: 5497853

Conclusion

Lithium was found in measureable quantities in the drinking waters of 22 of 27 county seats throughout the state of Texas. The incidence of patient's first admissions and prevalence of readmission as well as the diagnosis of psychosis, neurosis, and personality disorder to state mental hospitals from each of the counties was inversely proportional to the lithium content of their residential drinking water. We suggest that the quantity of lithium in the local drinking water may be dependent upon either the soil content or the amount leached from the soil and then diluted by the amount of rainfall in the region. There is a trend for lower lithium levels and greater prevalence of mental hospital admissions among residents in the eastern part of the state than in any other section of our state of Texas.

This study neither confirms nor refutes Cade's theory that lithium is an essential element. However, supportive evidence is presented that naturally occurring lithium exerts a measureable and statistically significant influence on the incidence of patients admitted to our state's mental hospitals and on the certain diagnostic categories of mental illness.

„Die Häufigkeit der Erstaufnahme von Patienten und die von Wiederaufnahmen sowie Diagnose von **Psychosen, Neurosen und Persönlichkeitsstörungen** in staatlichen psychiatrischen Kliniken waren **umgekehrt proportional zum Lithiumgehalt des Trinkwassers**.“

„Diese Studie weder bestätigt noch widerlegt sie [John]Cades Theorie, dass Lithium ein essentielles Element ist.
Sie liefert sie jedoch **überzeugende Beweise** dafür, dass **natürlich vorkommendes Lithium** einen messbaren und **statistisch signifikanten Einfluss** auf die Häufigkeit hat, mit der Patienten in diesem Bundesstaat in psychiatrische Kliniken eingewiesen werden, sowie **auf bestimmte diagnostische Kategorien psychischer**

Meta-Analysis > Aust N Z J Psychiatry. 2021 Feb;55(2):139-152. doi: 10.1177/0004867420963740. Epub 2020 Oct 13.

The association between lithium in drinking water and neuropsychiatric outcomes: A systematic review and meta-analysis from across 2678 regions containing 113 million people

Brenton Eyre-Watt [1], Eesharnan Mahendran [2], Shuichi Suetani [1 2 3 4], Joseph Firth [5 6], Steve Kisely [2 7], Dan Siskind [2 3 7]

Affiliations + expand

PMID: 33045847 DOI: 10.1177/0004867420963740

October 13, 2020

Abstract

Background: Lithium in drinking water may have significant mental health benefits. We investigated the evidence on the association between lithium concentrations in drinking water and their neuropsychiatric outcomes.

Methods: We conducted a systematic review and meta-analysis and searched Pubmed, Embase, Web of Science, PsycINFO and CINAHL up to 19 January 2020, for peer-reviewed research examining the association between lithium concentrations in drinking water and neuropsychiatric outcomes. We used a pairwise analysis and a random effects model to meta-analyse suicide rates and psychiatric hospital admissions. We assessed for publication bias using Egger's test and Duval and Tweedie's Trim and Fill analysis.

Results: Twenty-seven studies including 113 million subjects were included in this systematic review. Meta-analysis of 14 studies including 94 million people found higher lithium concentrations were associated with reduced suicide rates (r = -0.191, 95% confidence interval = [-0.287, -0.090], p < 0.001) and meta-analysis of two studies including 5 million people found higher lithium concentrations were associated with fewer hospital admissions (r = -0.413, 95% confidence interval = [-0.689, -0.031], p = 0.035). We found significant heterogeneity between studies (Q = 67.4, p < 0.001, I^2 = 80.7%) and the presence of publication bias (Egger's test; t value = 2.90, p = 0.013). Other included studies did not provide sufficient data to analyse other neuropsychiatric outcomes quantitatively.

Conclusion: Higher lithium concentrations in drinking water may be associated with reduced suicide rates and inpatient psychiatric admissions. The relationship with other neuropsychiatric outcomes and complications remains unclear. Further research is required before any public health recommendations can be made.**Trial registration number:** The study was registered with PROSPERO, number CRD42018090145.

„Höhere Lithiumkonzentrationen im Trinkwasser stehen möglicherweise mit einer verringerten Selbstmordrate sowie einer geringeren Zahl von Einweisungen in psychiatrische Kliniken in Verbindung.“

Comparative Study > Biol Trace Elem Res. 1990 May;25(2):105-13. doi: 10.1007/BF02990271.

Lithium in drinking water and the incidences of crimes, suicides, and arrests related to drug addictions

1990

G N Schrauzer [1], K P Shrestha

Affiliations + expand

PMID: 1699579 DOI: 10.1007/BF02990271

Abstract

Using data for 27 Texas counties from 1978-1987, it is shown that the incidence rates of suicide, homicide, and rape are significantly higher in counties whose drinking water supplies contain little or no lithium than in counties with water lithium levels ranging from 70-170 micrograms/L; the differences remain statistically significant (p less than 0.01) after corrections for population density.

Die Selbstmord-, Mord- und Vergewaltigungsraten sind in Landkreisen, deren Trinkwasser kaum oder gar kein Lithium enthält, deutlich höher als in Landkreisen, in denen die Lithiumwerte zwischen 70 und 170

Lithium in drinking water and crime rates in Japan: cross-sectional study

2020

Kentaro Kohno, Nobuyoshi Ishii, Hirofumi Hirakawa and Takeshi Terao

Background

In pharmacological doses, lithium successfully treats bipolar disorder and it can reduce violent crimes committed by individuals with this disorder.

Aims

To investigate whether naturally occurring lithium in drinking water lowers rates of violent crime in the general population.

Method

We examined lithium levels in the drinking water of the 274 municipalities of Kyushu Island in Japan and compared these with the crime rates in each municipality.

Results

We found that lithium levels were significantly and inversely associated with crime rates in 2009.

Conclusions

Our findings suggest that even very low levels of lithium in drinking water may play a role in reducing crime rates in the general population.

Keywords

Lithium; trace element; drinking water; crime; epidemiological study.

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[…] Lithiumspiegel im Trinkwasser steht in einem signifikanten umgekehrten Verhältnis zur Kriminalitätsrate […].
Unsere Ergebnisse deuten darauf hin, dass selbst sehr geringe Mengen Lithium im Trinkwasser die

Fraiha-Pegado *et al.*
International Journal of Bipolar Disorders (2024) 12:32
https://doi.org/10.1186/s40345-024-00348-5

International Journal of Bipolar Disorders

REVIEW **Open Access**

Trace lithium levels in drinking water and risk of dementia: a systematic review 2024

Julia Fraiha-Pegado[1], Vanessa J. Rodrigues de Paula[2], Tariq Alotaibi[1,3], Orestes Forlenza[2] and Tomas Hajek[1*]

Abstract

Background Since its debut in 1949, lithium (Li) has been regarded as a gold standard therapy for mood stabilization. Neuroprotective effects of Li have been replicated across many different paradigms ranging from tissue cultures to human studies. This has generated interest in potentially repurposing this drug. However, the optimal dosage required for neuroprotective effects remains unclear and may be different than the doses needed for treatment of bipolar disorders. Recent studies on trace-Li levels in the water suggest that Li, could slow cognitive decline and prevent dementia with long-term use even at very low doses. The current review aims to synthesize the data on the topic and challenge the conventional high-dose paradigm.

Results We systematically reviewed five available studies, which reported associations between trace-Li in water and incidence or mortality from dementia. Association between trace-Li levels and a lower risk or mortality from dementia were observed at concentrations of Li in drinking water as low as 0.002 mg/L and 0.056 mg/L. Meanwhile, levels below 0.002 mg/L did not elicit this effect. Although three of the five studies found dementia protective properties of Li in both sexes, a single study including lower Li levels (0.002 mg/l) found such association only in women.

Conclusion The reviewed evidence shows that trace-Li levels in the water are sufficient to lower the incidence or mortality from dementia. Considering the lack of options for the prevention or treatment of dementia, we should not ignore these findings. Future trials of Li should focus on long term use of low or even micro doses of Li in the prevention or treatment of dementia.

Keywords Neuroprotection, Lithium, Dementia, Micro dosing

Fünf unabhängige Studien:

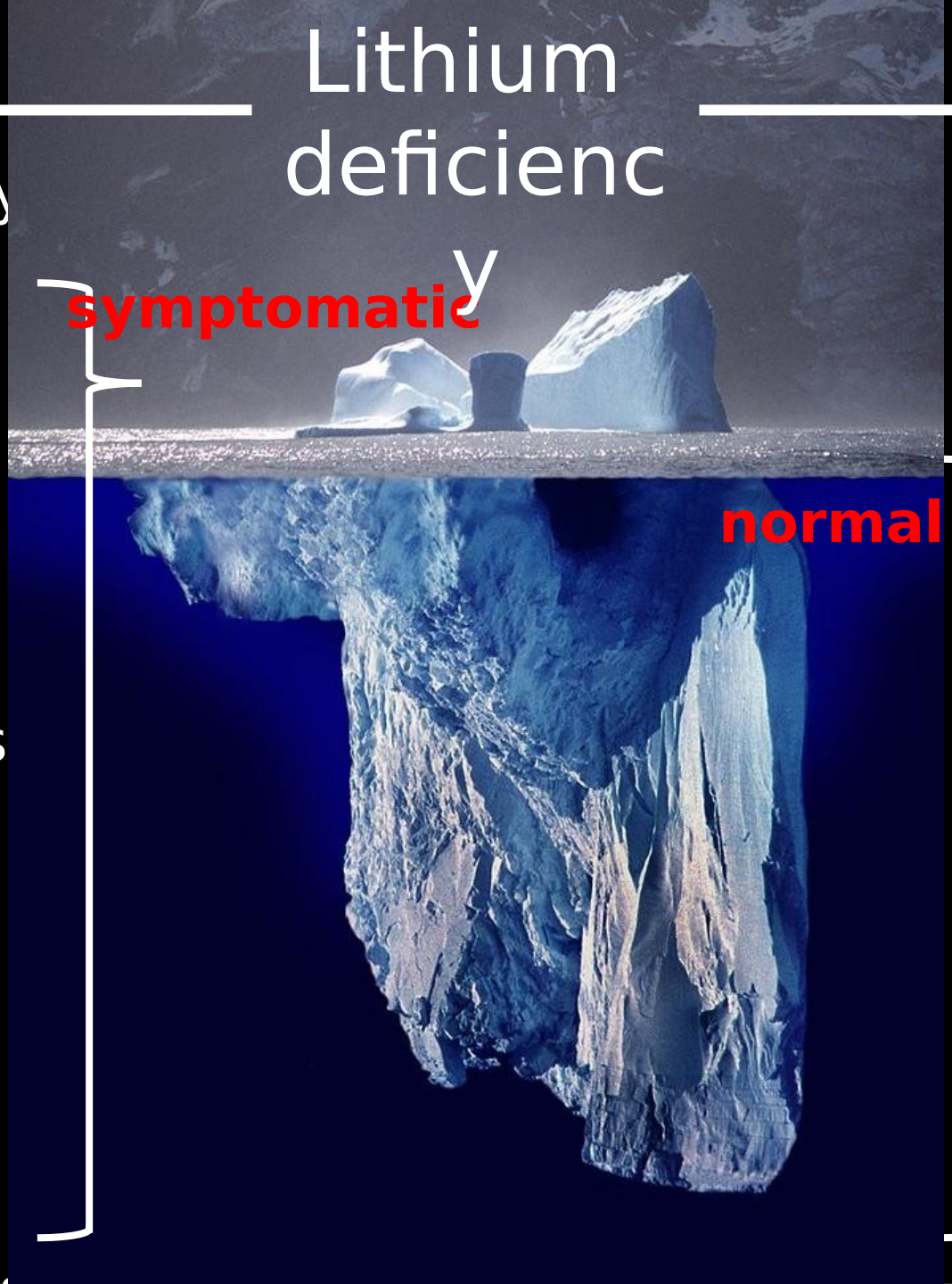
„Die überprüfte Evidenz zeigt, dass Spuren von Lithium im Trinkwasser ausreichen, **um die Häufigkeit oder Mortalität von Demenzerkrankungen zu senken**.“

„Angesichts des Mangels an Mitteln zur Vorbeugung oder Behandlung von Demenz

- Cardiovascular disease
- Cancer
- Reduced life expectancy

- High admission rate to psychiatric clinics
  - Schizophrenia
  - Psychosis
  - Neuroses
  - Bipolar disorder
  - Personality disorders
- Autism
- High depression & suizide rates
- Drug abuse
- Higher crime rates
  - Murder
  - Rape
- Higher Alzheimer's rate

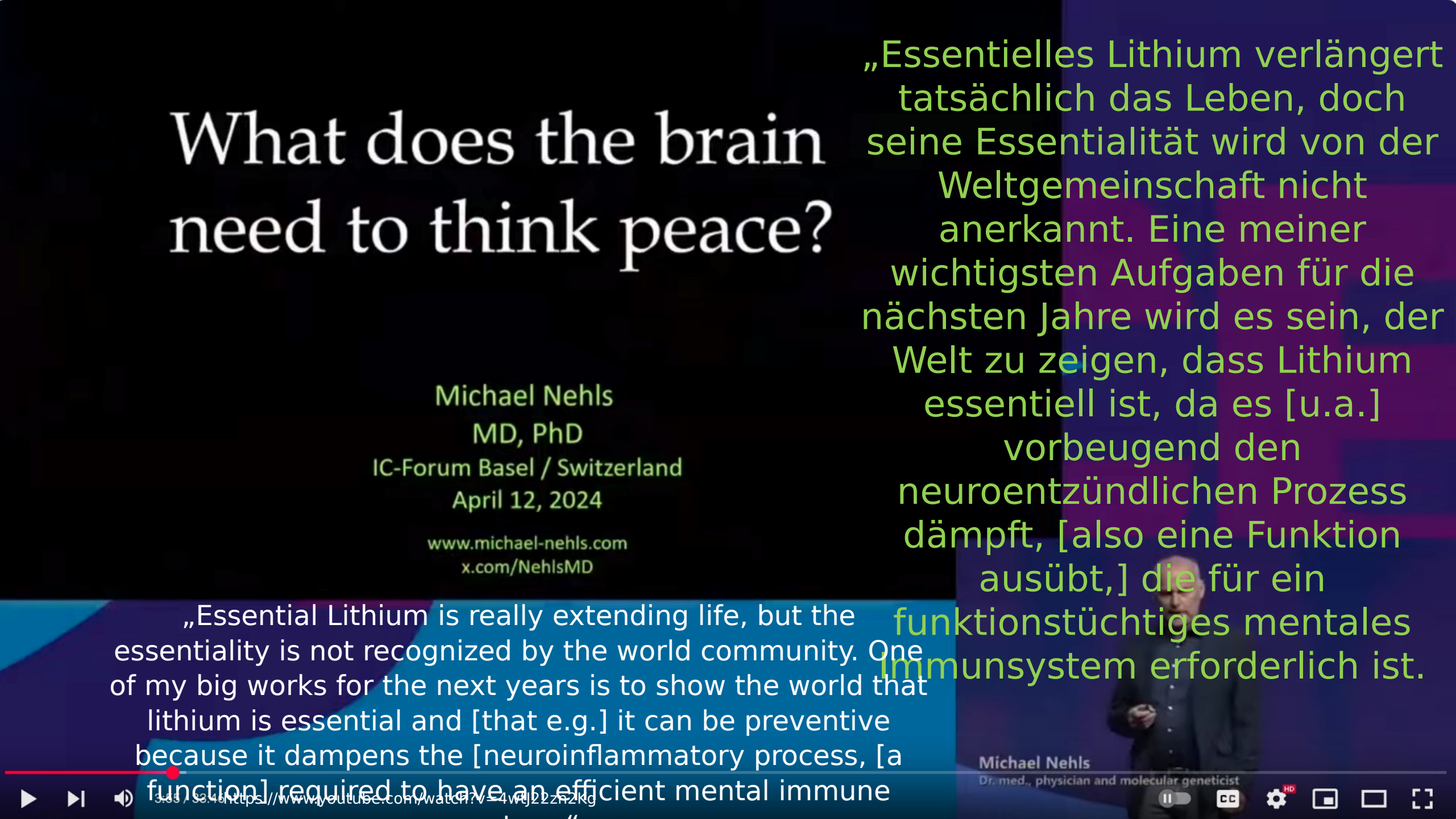
Lithium deficiency



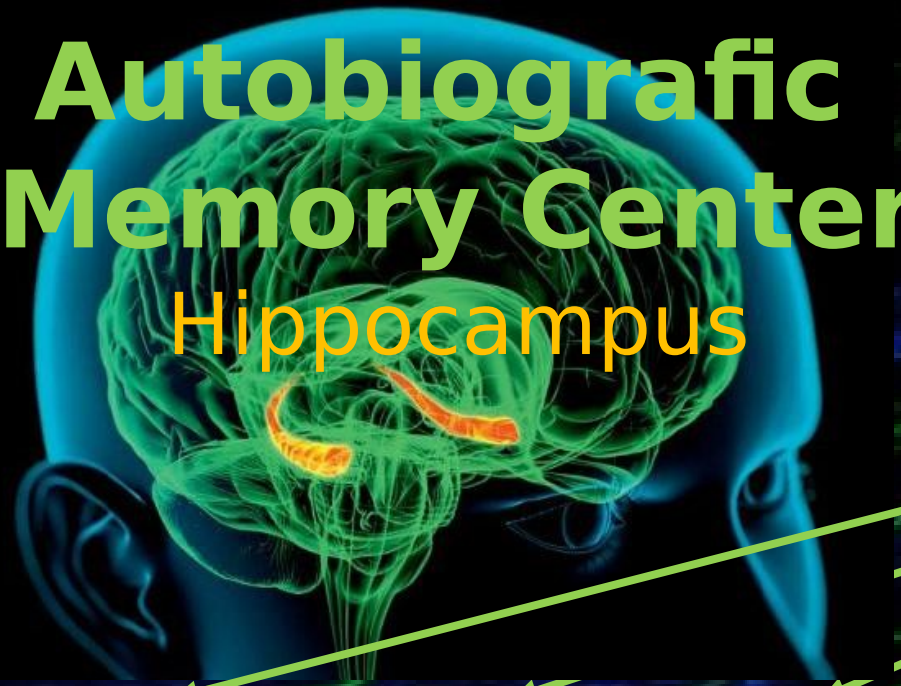
Mental immune system dysfunction

Compromized mental capacity to critical thinking, incl. thinking peace

Iceberg14.jpg|Or


What does the brain need to think peace?
Michael Nehls
MD, PhD
IC-Forum Basel / Switzerland
April 12, 2024
www.michael-nehls.com
x.com/NehlsMD
„Essentielles Lithium verlängert tatsächlich das Leben, doch seine Essentialität wird von der Weltgemeinschaft nicht anerkannt. Eine meiner wichtigsten Aufgaben für die nächsten Jahre wird es sein, der Welt zu zeigen, dass Lithium essentiell ist, da es [u.a.] vorbeugend den neuroentzündlichen Prozess dämpft, [also eine Funktion ausübt,] die für ein funktionstüchtiges mentales Immunsystem erforderlich ist.
„Essential Lithium is really extending life, but the essentiality is not recognized by the world community. One of my big works for the next years is to show the world that lithium is essential and [that e.g.] it can be preventive because it dampens the [neuroinflammatory process, [a function] required to have an efficient mental immune
Michael Nehls
Dr. med., physician and molecular geneticist

Autobiografic Memory Center



Center of the Mental Immune System

autobiografic memory

critical thinking

resilience & curiosity

experience & individuality

creativity & planing

rational compassion

social competences

Adult hippocampal neurogenesis

Mental health up to the highest age

(Transgenerational support, longevity, and protection against AD)

Nehls *Journal of Molecular Psychiatry* (2016) 4:3
DOI 10.1186/s40303-016-0018-8

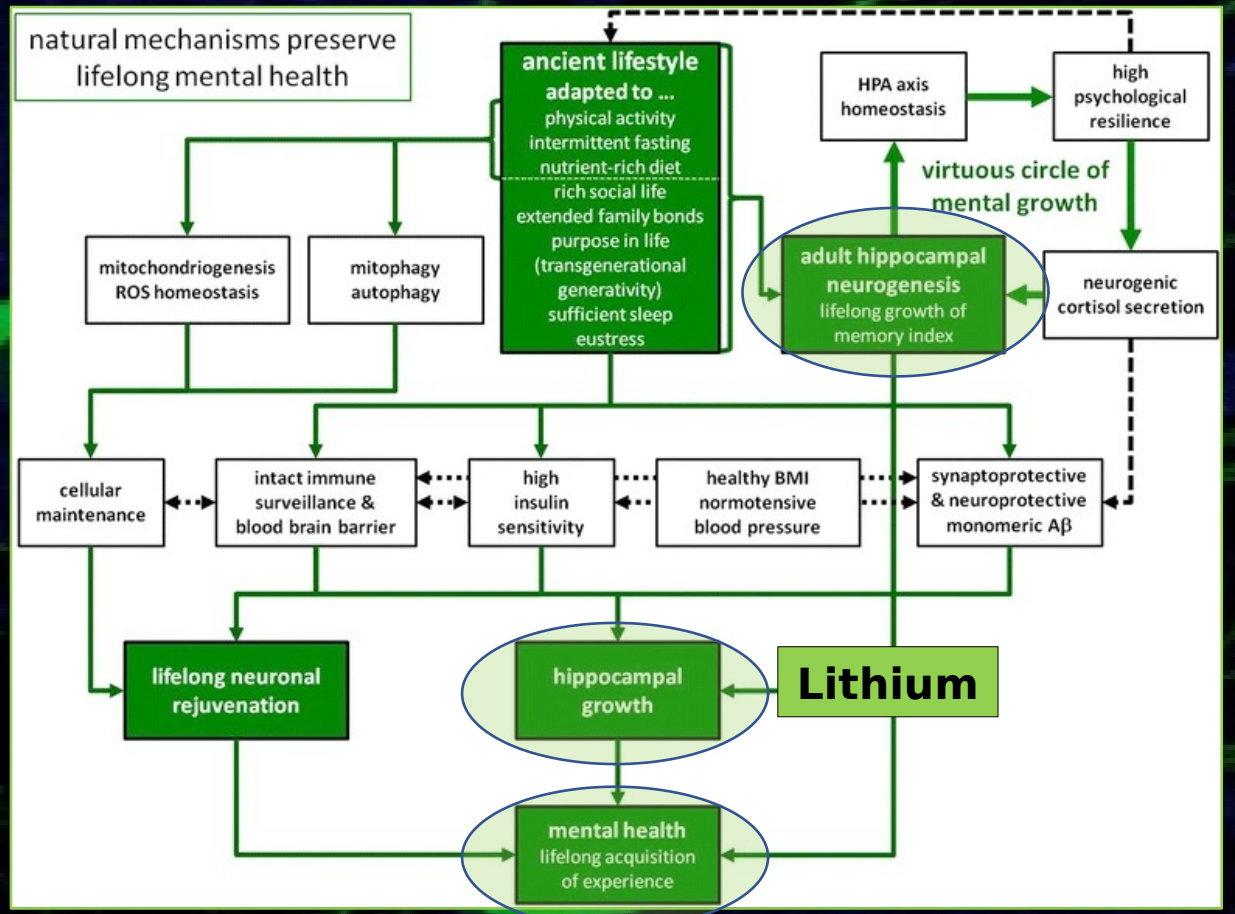
Journal of Molecular Psychiatry

July 15, 2016

REVIEW Open Access

Unified theory of Alzheimer's disease (UTAD): implications for prevention and curative therapy

Michael Nehls



PLoS One. 2010 Dec 20;5(12):e14382. doi: 10.1371/journal.pone.0014382.

Lithium improves hippocampal neurogenesis, neuropathology and cognitive functions in APP mutant mice

Anna Fiorentini [1], Maria Cristina Rosi, Cristina Grossi, Ilaria Luccarini, Fiorella Casamenti

Affiliations – collapse

Affiliation

1 Department of Pharmacology, University of Florence, Florence, Italy.

PMID: 21187954 PMCID: PMC3004858 DOI: 10.1371/journal.pone.0014382

Randomized Controlled Trial J Alzheimers Dis. 2009;16(3):649-56. doi: 10.3233/JAD-2009-1004.

Increase of BDNF serum concentration in lithium treated patients with early Alzheimer's disease

Thomas Leyhe [1], Gerhard W Eschweiler, Elke Stransky, Thomas Gasser, Peter Annas, Hans Basun, Christoph Laske

Affiliations – collapse

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1 Department of Psychiatry and Psychotherapy, University of Tübingen, Tübingen, Germany. thomas.leyhe@med.uni-tuebingen.de

PMID: 19276559 DOI: 10.3233/JAD-2009-1004

Lithium activates adult hippocampal neurogenesis (i.e. Alzheimer-

Neurogenic Region-Selectiv
Lithium Uptake

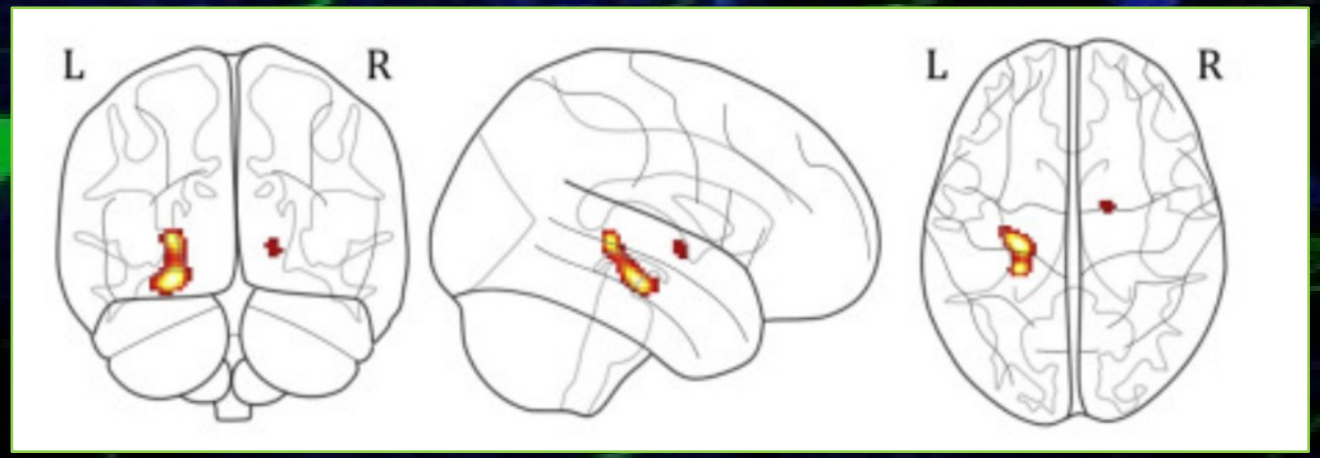
› Biol Psychiatry. 2020 Sep 1;88(5):426-433. doi: 10.1016/j.biopsych.2020.02.1181. Epub 2020 Mar 6.

Accumulation of Lithium in the Hippocampus of Patients With Bipolar Disorder: A Lithium−7 Magnetic Resonance Imaging Study at 7 Tesla

Jacques Stout [1], Franz Hozer [2], Arthur Coste [1], Franck Mauconduit [3], Nouzha Djebrani-Oussedik [4], Samuel Sarrazin [1], Joel Poupon [4], Manon Meyrel [5], Sandro Romanzetti [6], Bruno Etain [7], Cécile Rabrait-Lerman [1], Josselin Houenou [8], Frank Bellivier [7], Edouard Duchesnay [1], Fawzi Boumezbeur [9]

Affiliations + expand

PMID: 32340717 DOI: 10.1016/j.biopsych.2020.02.1181



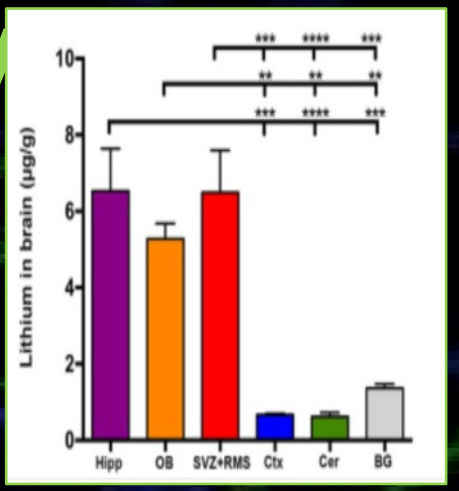
› Sci Rep. 2017 Jan 18:7:40726. doi: 10.1038/srep40726.

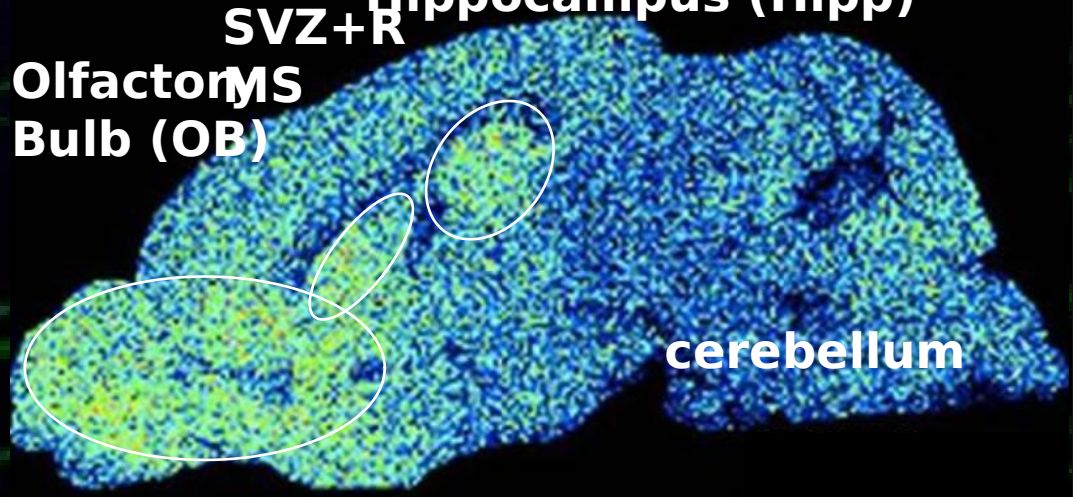
Lithium Accumulates in Neurogenic Brain Regions as Revealed by High Resolution Ion Imaging

Giulia Zanni [1,2], Wojciech Michno [3,4], Elena Di Martino [1], Anna Tjärnlund-Wolf [2], Jean Pettersson [5], Charlotte Elizabeth Mason [1], Gustaf Hellspong [1], Klas Blomgren [1,6], Jörg Hanrieder [3,4,7,8]

Affiliations + expand

PMID: 28098178 PMCID: PMC5241875 DOI: 10.1038/srep40726





Lithium activates adult hippocampal neurogenesis (which is

Nehls *Journal of Molecular Psychiatry* (2016) 4:3
DOI 10.1186/s40303-016-0018-8

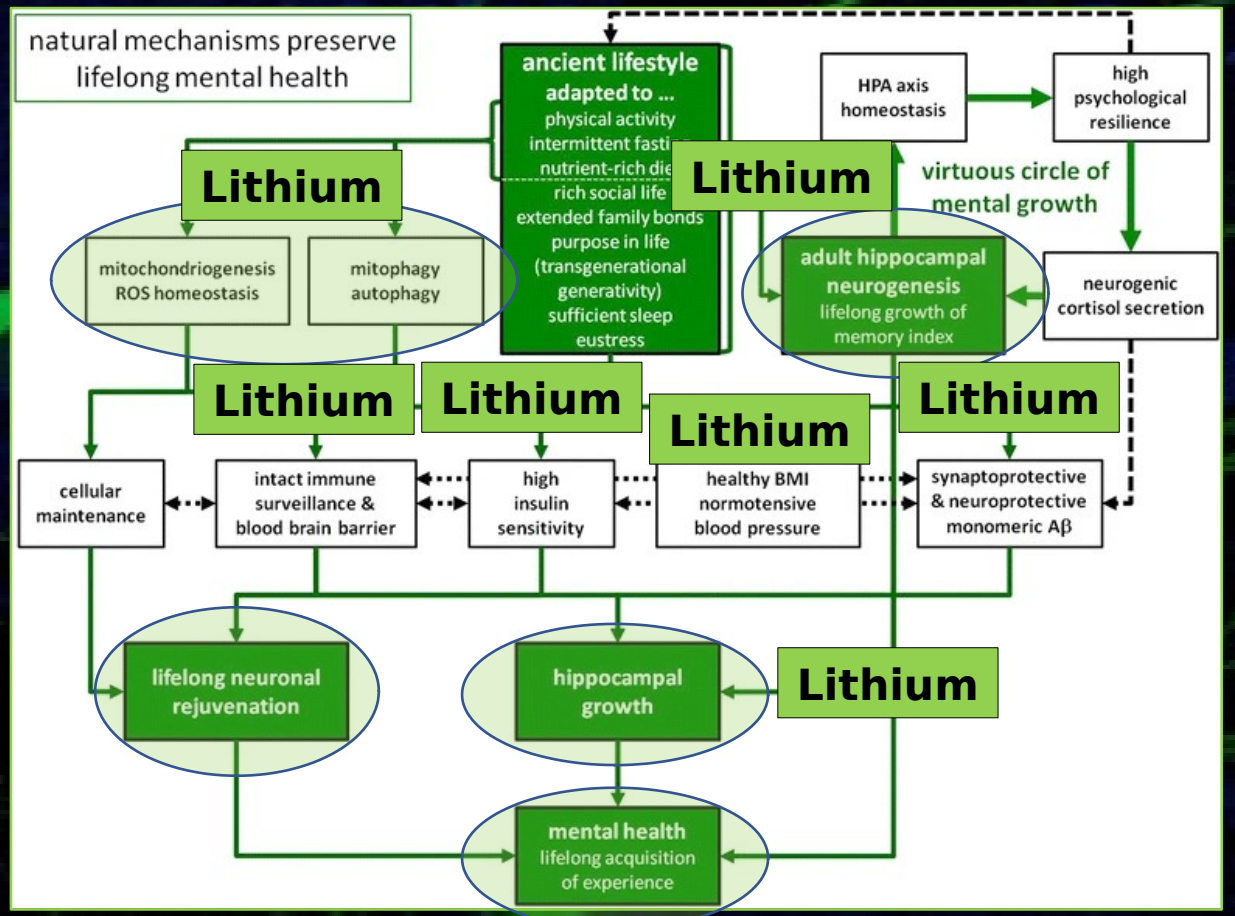
Journal of Molecular Psychiatry

July 15, 2016

REVIEW Open Access

Unified theory of Alzheimer's disease (UTAD): implications for prevention and curative therapy

Michael Nehls



frontiers in Cell and Developmental Biology

REVIEW
published: 04 March 2020
doi: 10.3389/fcell.2020.00138

March 4, 2020

Autophagie und Stammzellen: Selbstverzehr zur Selbsterneuerung

*Natasha C. Chang**

Department of Biochemistry, Faculty of Medicine, McGill University, Montreal, QC, Canada

Autophagy is a fundamental cell survival mechanism that allows cells to adapt to metabolic stress through the degradation and recycling of intracellular components to generate macromolecular precursors and produce energy. The autophagy pathway is critical for development, maintaining cellular and tissue homeostasis, as well as immunity and prevention of human disease. Defects in autophagy have been attributed to cancer, neurodegeneration, muscle and heart disease, infectious disease, as well as aging. While autophagy has classically been viewed as a passive quality control and general house-keeping mechanism, emerging evidence demonstrates that autophagy is an active process that regulates the metabolic status of the cell. Adult stem cells, which are long-lived cells that possess the unique ability to self-renew and differentiate into specialized cells throughout the body, have distinct metabolic requirements. Research in a variety of stem cell types have established that autophagy plays critical roles in stem cell quiescence, activation, differentiation, and self-renewal. Here, we will review the evidence demonstrating that autophagy is a key regulator of stem cell function and how defective stem cell autophagy contributes to degenerative disease, aging and the generation of cancer stem cells. Moreover, we will discuss the merits of targeting autophagy as a regenerative medicine strategy to promote stem cell function and improve stem cell-based therapies.

OPEN ACCESS

Edited by:
Anthony Scimè,
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Reviewed by:
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Hong Kong University of Science and Technology, Hong Kong
Ayako Nakamura-Ishizu,
Tokyo Women's Medical University,

„Autophagie ist ein fundamentaler Überlebensmechanismus von Zellen. […] Defekte in der Autophagie werden mit Krebs, Neurodegeneration, Muskel- und Herzerkrankungen, Infektionskrankheiten

Lithium stimuliert die Autophagie durch Hemmung der Inositolmonophosphatase.

2005

Lithium induces autophagy by inhibiting inositol monophosphatase (IMPase)

Sovan Sarkar,[1] R. Andres Floto,[2] Zdenek Berger,[1,3] Sara Imarisio,[1,3] Axelle Cordenier,[1,3] Matthieu Pasco,[3] Lynnette J. Cook,[1] and David C. Rubinsztein[1]

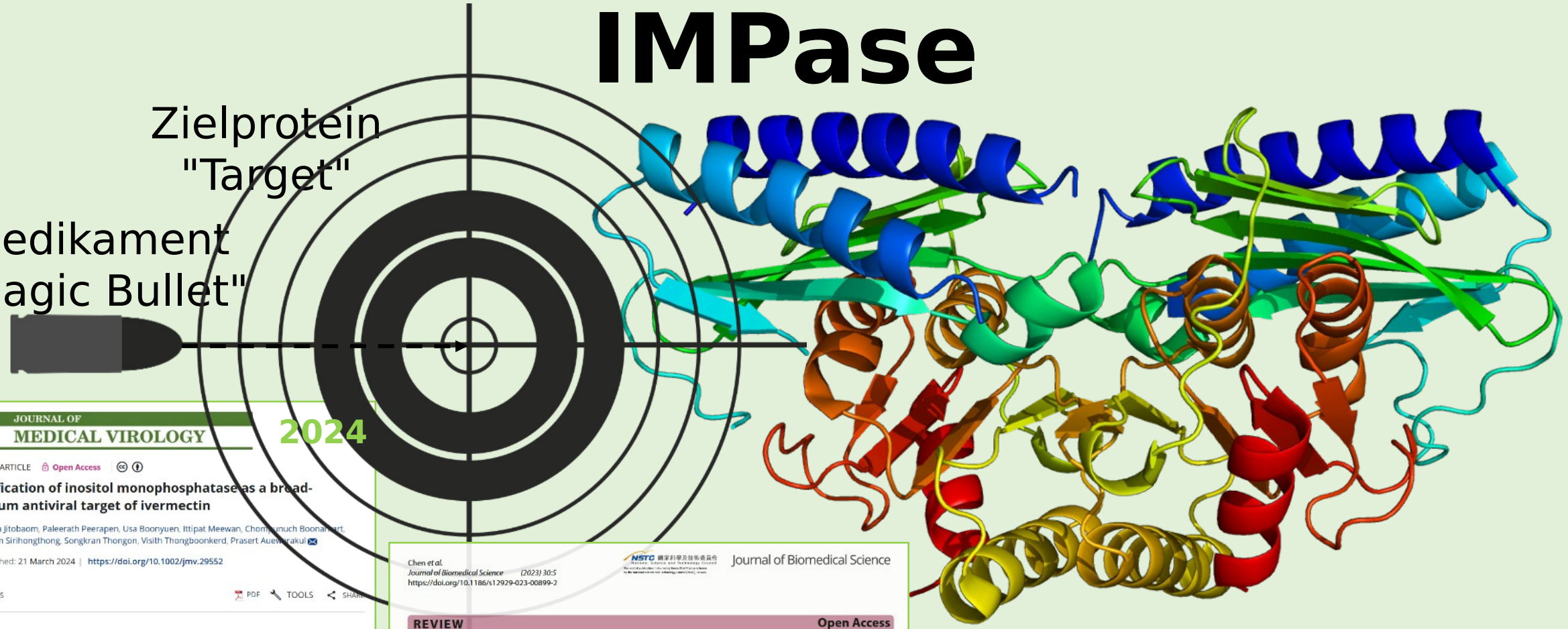
[1]Department of Medical Genetics and [2]Department of Medicine, University of Cambridge, Cambridge Institute for Medical Research, Addenbrooke's Hospital, Cambridge CB2 2XY, England, UK
[3]Department of Genetics, University of Cambridge, Cambridge CB2 3EH, England, UK

Macroautophagy is a key pathway for the clearance of aggregate-prone cytosolic proteins. Currently, the only suitable pharmacologic strategy for up-regulating autophagy in mammalian cells is to use rapamycin, which inhibits the mammalian target of rapamycin (mTOR), a negative regulator of autophagy. Here we describe a novel mTOR-independent pathway that regulates autophagy. We show that lithium induces autophagy, and thereby, enhances the clearance of autophagy substrates, like mutant huntingtin and α-synucleins. This effect is not mediated by glycogen synthase kinase 3β inhibition. The autophagy-enhancing properties of lithium were mediated by inhibition of inositol monophosphatase and led to free inositol depletion. This, in turn, decreased myo-inositol-1,4,5-triphosphate (IP_3) levels. Our data suggest that the autophagy effect is mediated at the level of (or downstream of) lowered IP_3, because it was abrogated by pharmacologic treatments that increased IP_3. This novel pharmacologic strategy for autophagy induction is independent of mTOR, and may help treatment of neurodegenerative diseases, like Huntington's disease, where the toxic protein is an autophagy substrate.

IMPase

Zielprotein
"Target"

Medikament
"Magic Bullet"



JOURNAL OF MEDICAL VIROLOGY

2024

RESEARCH ARTICLE Open Access

Identification of inositol monophosphatase as a broad-spectrum antiviral target of ivermectin

Kunlakanya Jitobaom, Paleerath Peerapen, Usa Boonyuen, Ittipat Meewan, Chonticha Boonarkart, Thanyaporn Sirihongthong, Songkran Thongon, Visith Thongboonkerd, Prasert Auewarakul

First published: 21 March 2024 | https://doi.org/10.1002/jmv.29552

SECTIONS PDF TOOLS SHARE

Identifizierung von Inositolmonophosphatase als antivirales Zielmolekül (Target) mit breitem Wirk-

Ivermectin is a lithium-mimetic!

Chen et al.
Journal of Biomedical Science (2023) 30:5
https://doi.org/10.1186/s12929-023-00899-2

Journal of Biomedical Science

REVIEW Open Access

The role of autophagy in viral infections

Tong Chen[1,2], Shaoyu Tu[1,2], Ling Ding[1,2], Meilin Jin[1,2], Huanchun Chen[1,2] and Hongbo Zhou[1,2*]

2023

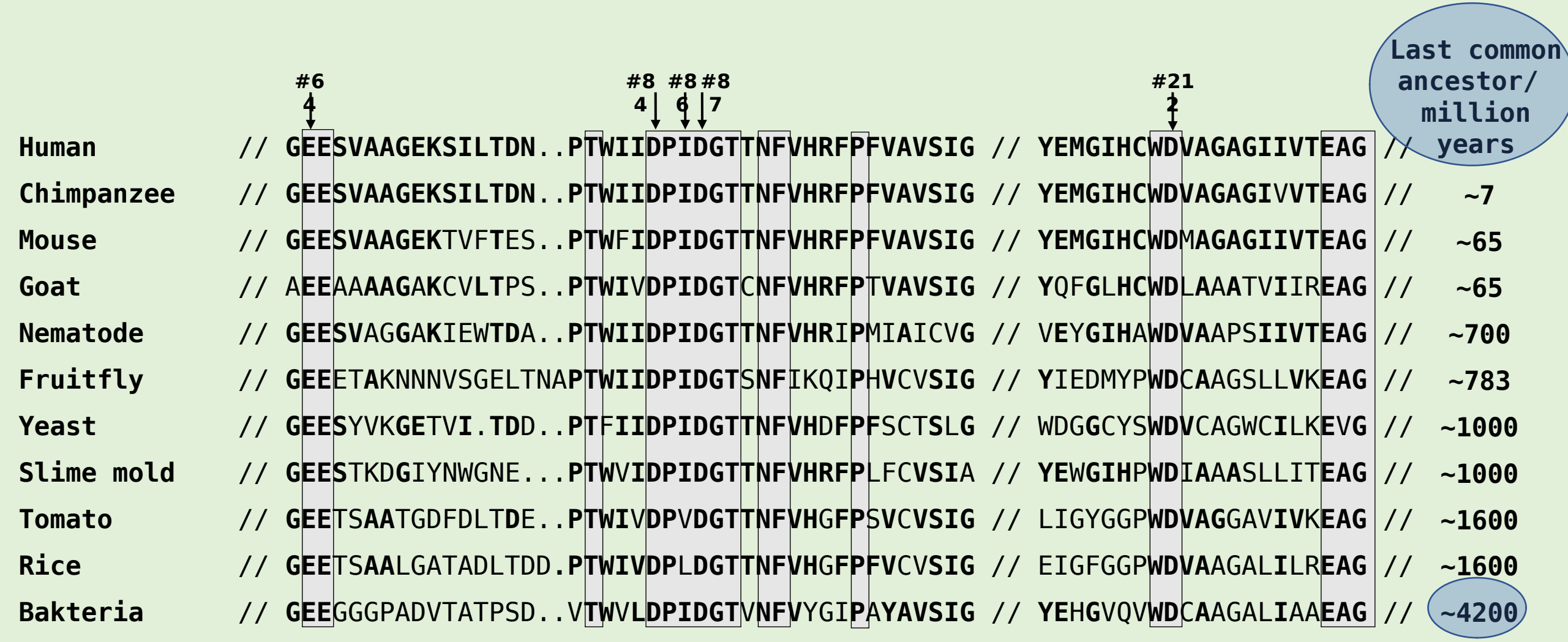
Abstract

Autophagy is an evolutionarily conserved catabolic cellular process that exerts antiviral functions during viral invasion. However, co-evolution and co-adaptation between viruses and autophagy have armed viruses with multiple strategies to subvert the autophagic machinery and counteract cellular antiviral responses. Specifically, the host cell quickly initiates the autophagy to degrade virus particles or virus components upon a viral infection, while coop-

Autophagy is an evolutionarily conserved catabolic cellular process that exerts antiviral functions during a viral invasion.

„Autophagie ist ein **evolutionär konservierter,** kataboler Zellprozess, der während einer Virusinvasion antivirale Funktionen ausübt.“

IMPase


#6
4
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4
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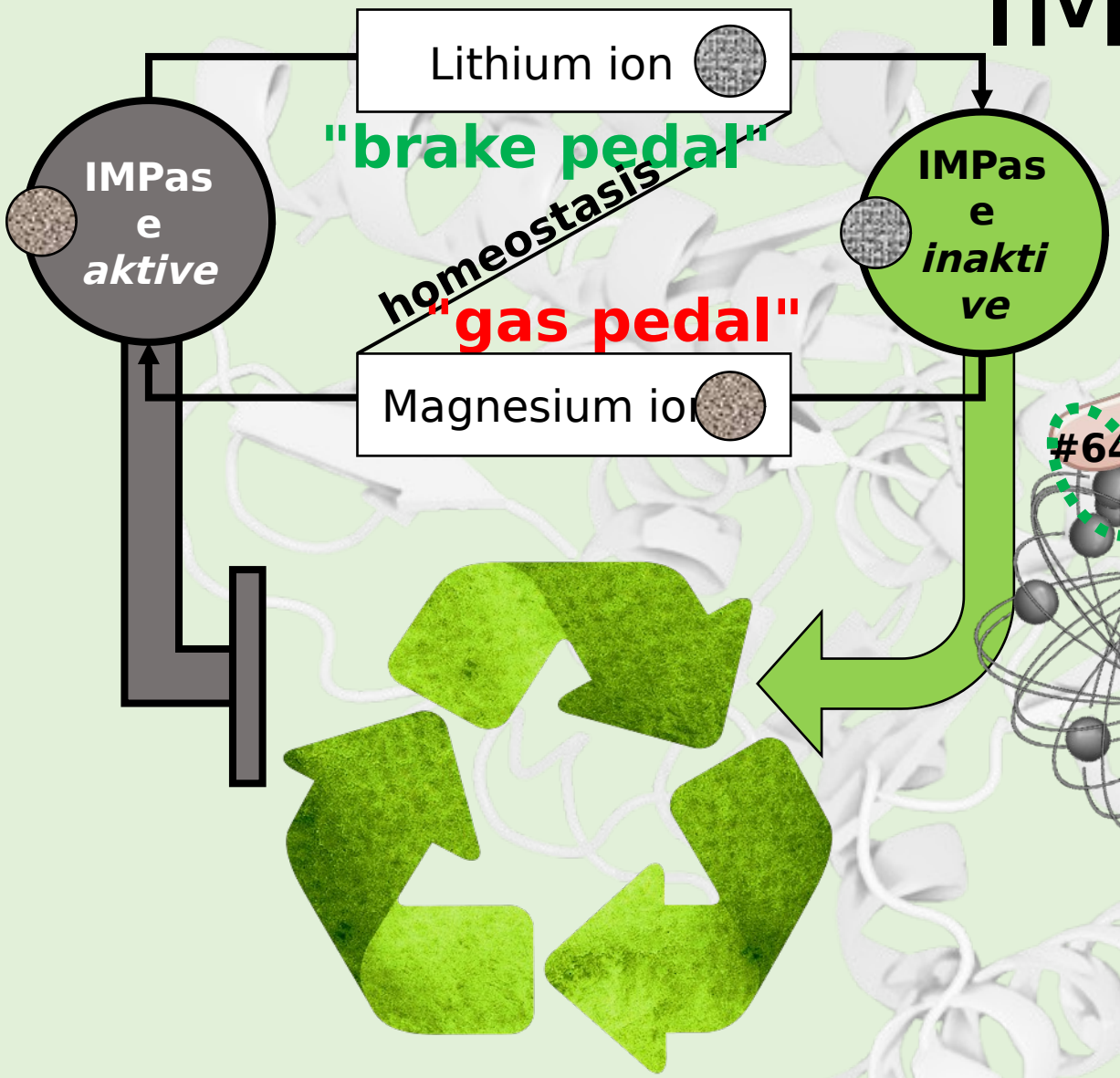
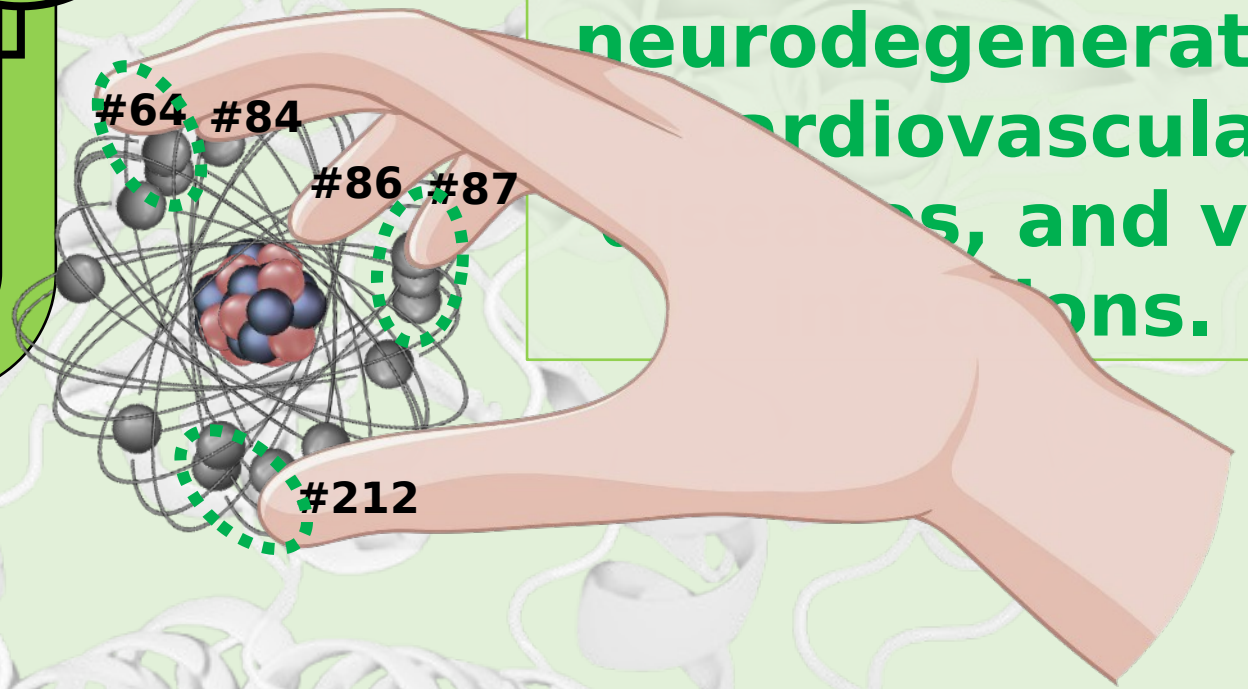
6
#8
7
#21
2
Last common ancestor/ million years
Human // GEESVAAGEKSILTDN..PTWIIDPIDGTTNFVHRFPFVAVSIG // YEMGIHCWDVAGAGIIVTEAG //
Chimpanzee // GEESVAAGEKSILTDN..PTWIIDPIDGTTNFVHRFPFVAVSIG // YEMGIHCWDVAGAGIVVTEAG // ~7
Mouse // GEESVAAGEKTVFTES..PTWFIDPIDGTTNFVHRFPFVAVSIG // YEMGIHCWDMAGAGIIVTEAG // ~65
Goat // AEEAAAAGAKCVLTPS..PTWIVDPIDGTCNFVHRFPTVAVSIG // YQFGLHCWDLAAATVIIREAG // ~65
Nematode // GEESVAGGAKIEWTDA..PTWIIDPIDGTTNFVHRIPMIAICVG // VEYGIHAWDVAAPSIIVTEAG // ~700
Fruitfly // GEEETAKNNNVSGELTNAPTWIIDPIDGTSNFIKQIPHVCVSIG // YIEDMYPWDCAAGSLLVKEAG // ~783
Yeast // GEESYVKGETVI.TDD..PTFIIDPIDGTTNFVHDFPFSCTSLG // WDGGCYSWDVCAGWCILKEVG // ~1000
Slime mold // GEESTKDGIYNWGNE...PTWVIDPIDGTTNFVHRFPLFCVSIA // YEWGIHPWDIAAASLLITEAG // ~1000
Tomato // GEETSAATGDFDLTDE..PTWIVDPVDGTTNFVHGFPSVCVSIG // LIGYGGPWDVAGGAVIVKEAG // ~1600
Rice // GEETSAALGATADLTDD.PTWIVDPLDGTTNFVHGFPFVCVSIG // EIGFGGPWDVAAGALILREAG // ~1600
Bakteria // GEEGGGPADVTATPSD..VTWVLDPIDGTVNFVYGIPAYAVSIG // YEHGVQVWDCAAGALIAAEAG // ~4200

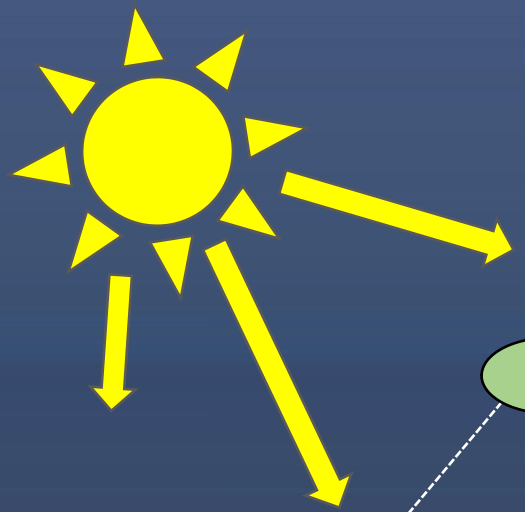
IMPase





Autophagy is naturally activated by lithium, which reduces the risk of cancer, neurodegeneration, rdiovascular s, and viral ons.

LUCA *Last Universal Common Ancestor*
4.2 billion years



Ur-Prokaryot
(mit Zellwand)

Ur-Eukaryot
(mit Zellmembran)

CO_2

Reich der
Bakterien

O_2

Zellkern

Zellkern
Chloroplast
Mitochondrium

Mitochondrium
Zellkern

Mikroalge
(mit Zellwand)
z.B. *Chlorella*

Mikropilz
(mit Zellwand)
z.B. *Saccharomyces*

Mitochondrium
Zellkern

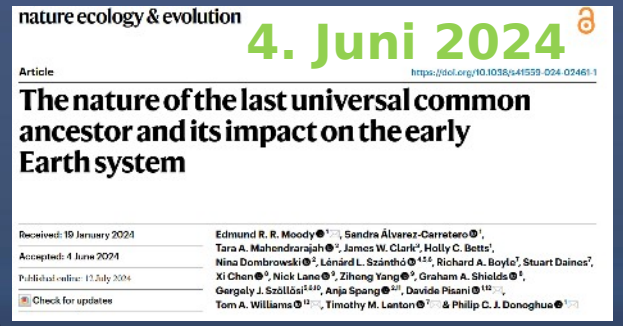
Kingdom of
Plants

Kingdom of
Fungi

Kingdom of
Protists

Reich der
Tiere

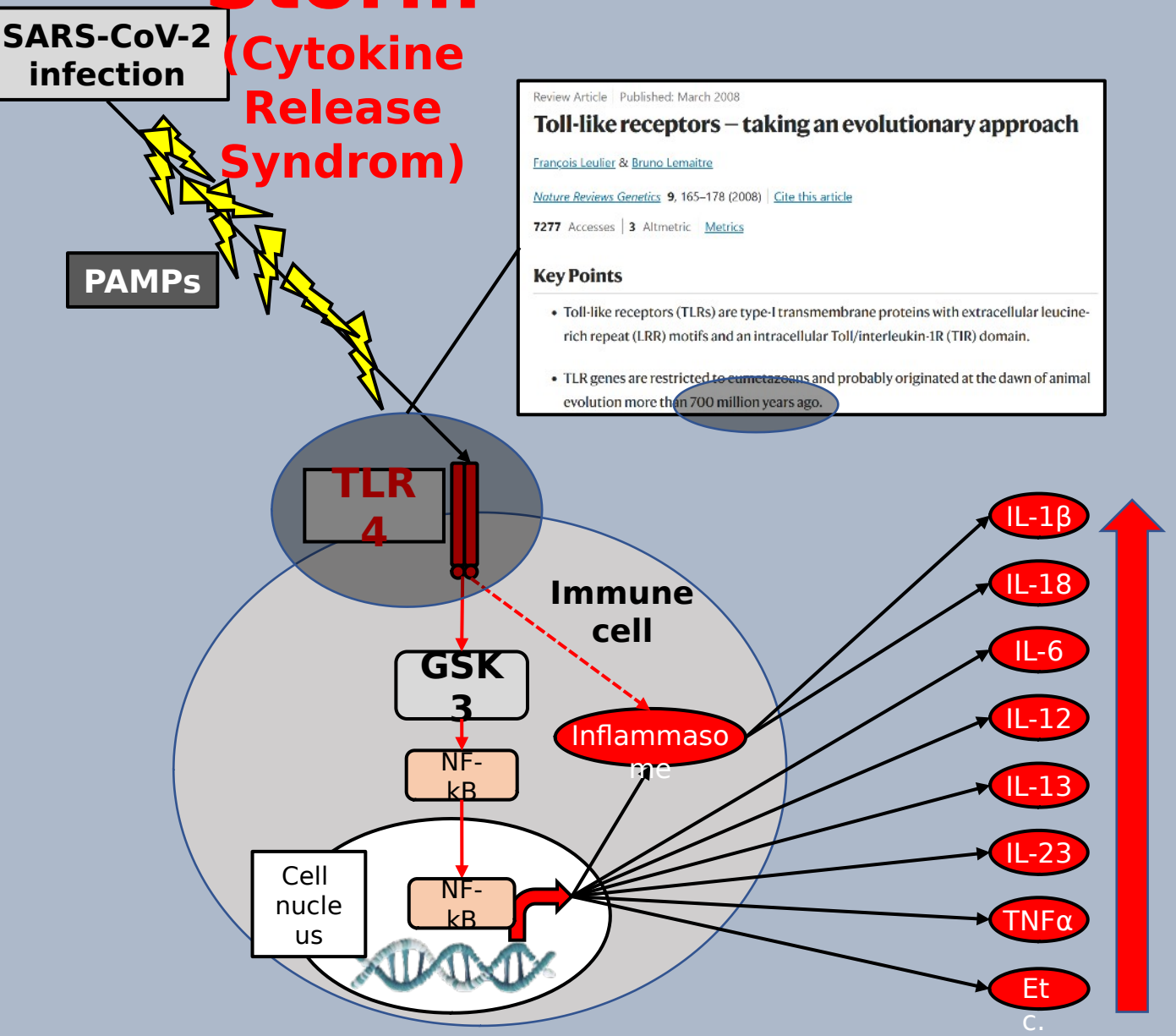
"tierische"
Einzeller
(mit Zellmembran)



LUCA possessed an early immune system […] already involved in an arms race with viruses."

„LUCA besaß ein frühen Immunsystem […],
und befand sich in einem Wettrüsten mit Viren."

Cytokine Storm (Cytokine Release Syndrom)



Review Article | Published: March 2008

Toll-like receptors – taking an evolutionary approach

François Leulier & Bruno Lemaitre

Nature Reviews Genetics 9, 165–178 (2008) | Cite this article

7277 Accesses | 3 Altmetric | Metrics

Key Points

- Toll-like receptors (TLRs) are type-I transmembrane proteins with extracellular leucine-rich repeat (LRR) motifs and an intracellular Toll/interleukin-1R (TIR) domain.
- TLR genes are restricted to eumetazoans and probably originated at the dawn of animal evolution more than 700 million years ago.

May 11, 2020 EJR European Journal of Rheumatology

Eur J Rheumatol. 2020 May 11;7(Suppl 2):S97–S98. doi: 10.5152/eurjrheum.2020.2062

Understanding the cytokine storm during COVID-19: Contribution of preexisting chronic inflammation

Pierre Miossec [1,✉]

Author information · Article notes · Copyright and License information

PMCID: PMC7431332 PMID: 32412405

The deregulation of this physiological inflammatory response in some patients with the SARS-CoV-2 infection is the cytokine storm with increased levels of these cytokines in the circulation (6). This syndrome was first described while treating some cancers with activated lymphocytes and/or large doses of cytokines (IL-2) (7). More recently, the same picture has been observed in patients treated with chimeric antigen receptor (CAR)T cells. Probably the best characterization was observed when normal individuals were exposed to a new agonistic anti-CD28 antibody; a very severe syndrome developed in a few hours (8). These examples show that the cytokine storm in COVID-19 results from inflammation, rather than from the virus itself. This information is critical when it comes to the selection of the treatments.

„[…] der Zytokinsturm bei schweren COVID-19-Verläufen resultiert eher aus der Entzündung, als aus dem Virus selbst. Diese Information ist entscheidend für die Auswahl der Behandlungsmethode.“

Cytokine Storm (Cytokine Release Syndrom)

SARS-CoV-2 infection

PAMPs

Vit D / VDR

TLR 4

Vit D / VDR

GSK 3

Vit D / VDR

NF-kB

Immune cell

Inflammasome

Cell nucleus

NF-kB

IL-1β

IL-18

IL-6

IL-12

IL-13

IL-23

TNFα

Et c.

Home > Aging Clinical and Experimental Research > Article

Evidence for possible association of vitamin D status with cytokine storm and unregulated inflammation in COVID-19 patients

Original Article | Open access | Published: 02 September 2020

Volume 32, pages 2141–2158, (2020) Cite this article

September 2, 202

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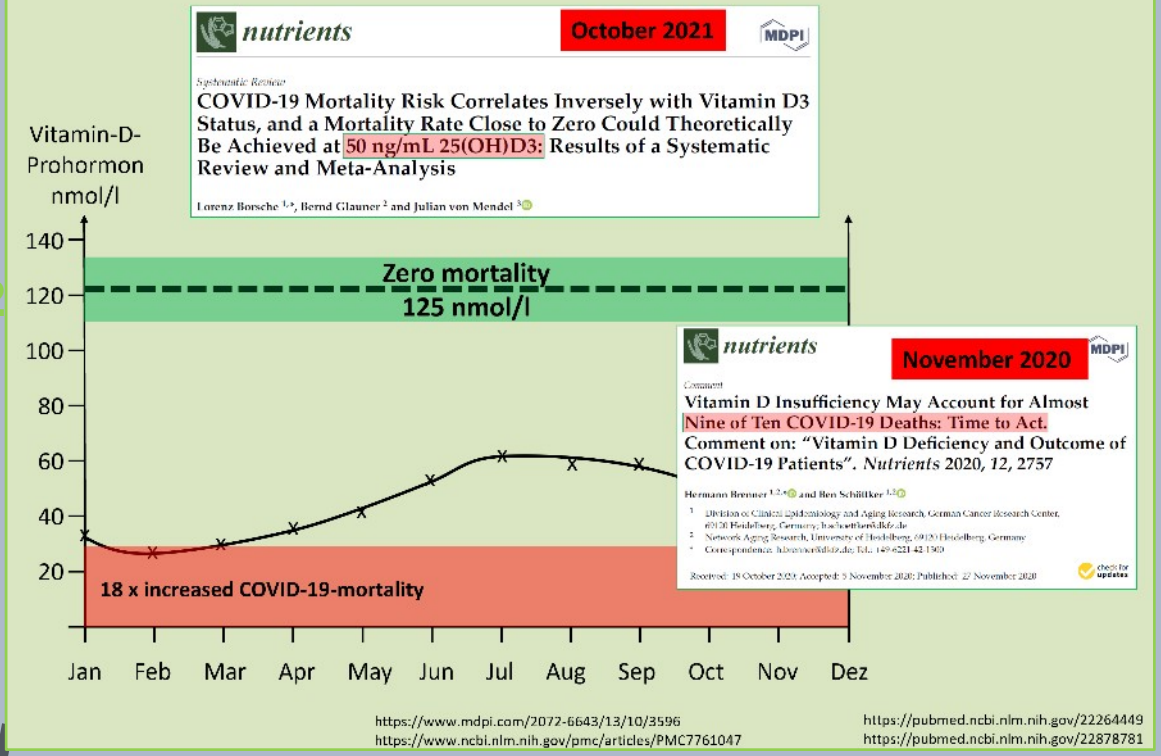
Ali Daneshkhah, Vasundhara Agrawal, Adam Eshein, Hariharan Subramanian, Hemant Kumar Roy & Vadim Backman



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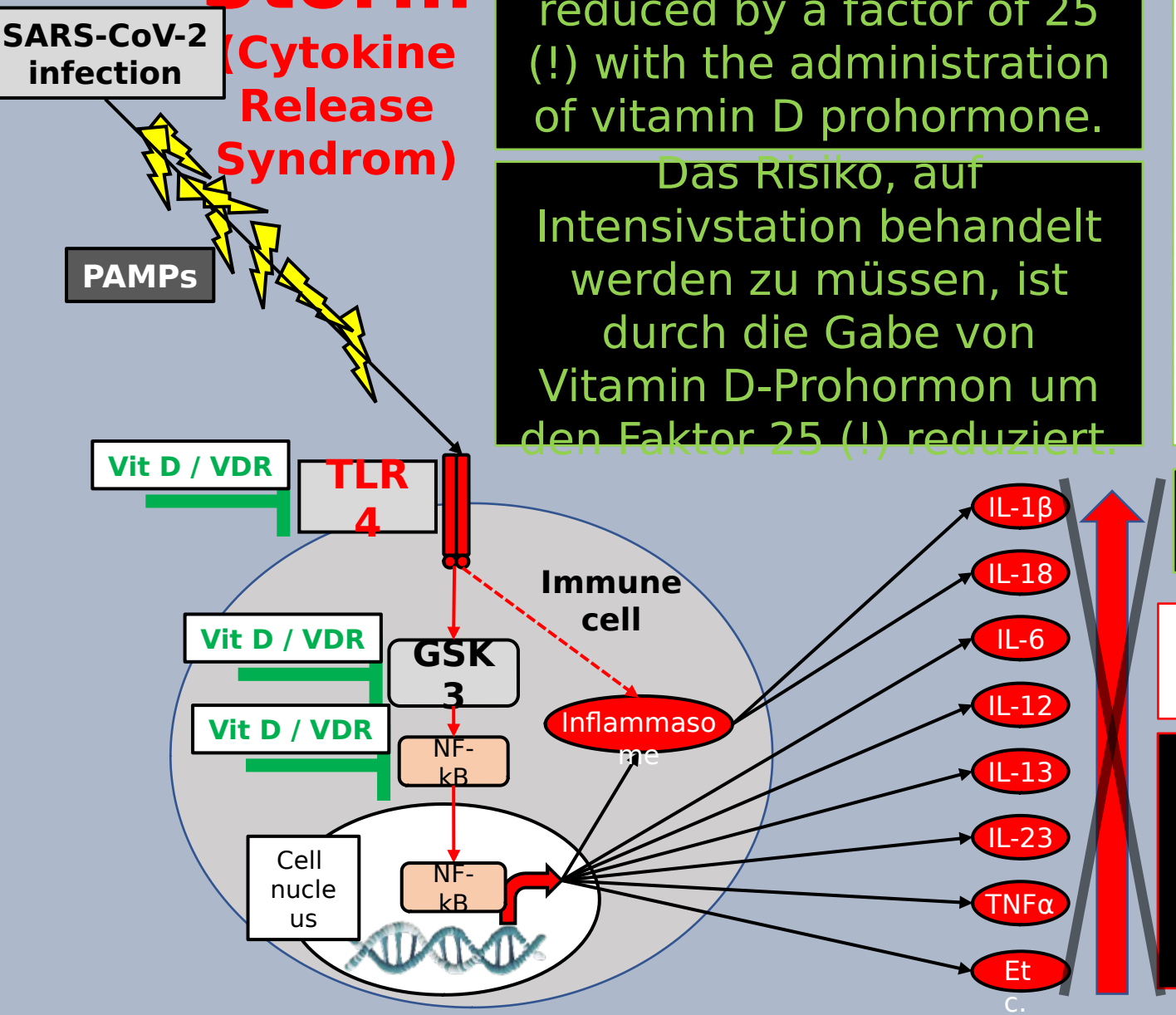
Cytokine Storm (Cytokine Release Syndrom)

The risk of requiring intensive care treatment is reduced by a factor of 25 (!) with the administration of vitamin D prohormone.

Das Risiko, auf Intensivstation behandelt werden zu müssen, ist durch die Gabe von Vitamin D-Prohormon um den Faktor 25 (!) reduziert.



Contents lists available at ScienceDirect

Journal of Steroid Biochemistry and Molecular Biology

journal homepage: www.elsevier.com/locate/jsbmb

August 29, 2020

"Effect of calcifediol treatment and best available therapy versus best available therapy on intensive care unit admission and mortality among patients hospitalized for COVID-19: A pilot randomized clinical study"

Marta Entrenas Castillo [a], Luis Manuel Entrenas Costa [a,*], José Manuel Vaquero Barrios [a], Juan Francisco Alcalá Díaz [b], José López Miranda [b], Roger Bouillon [c], José Manuel Quesada Gomez [d]

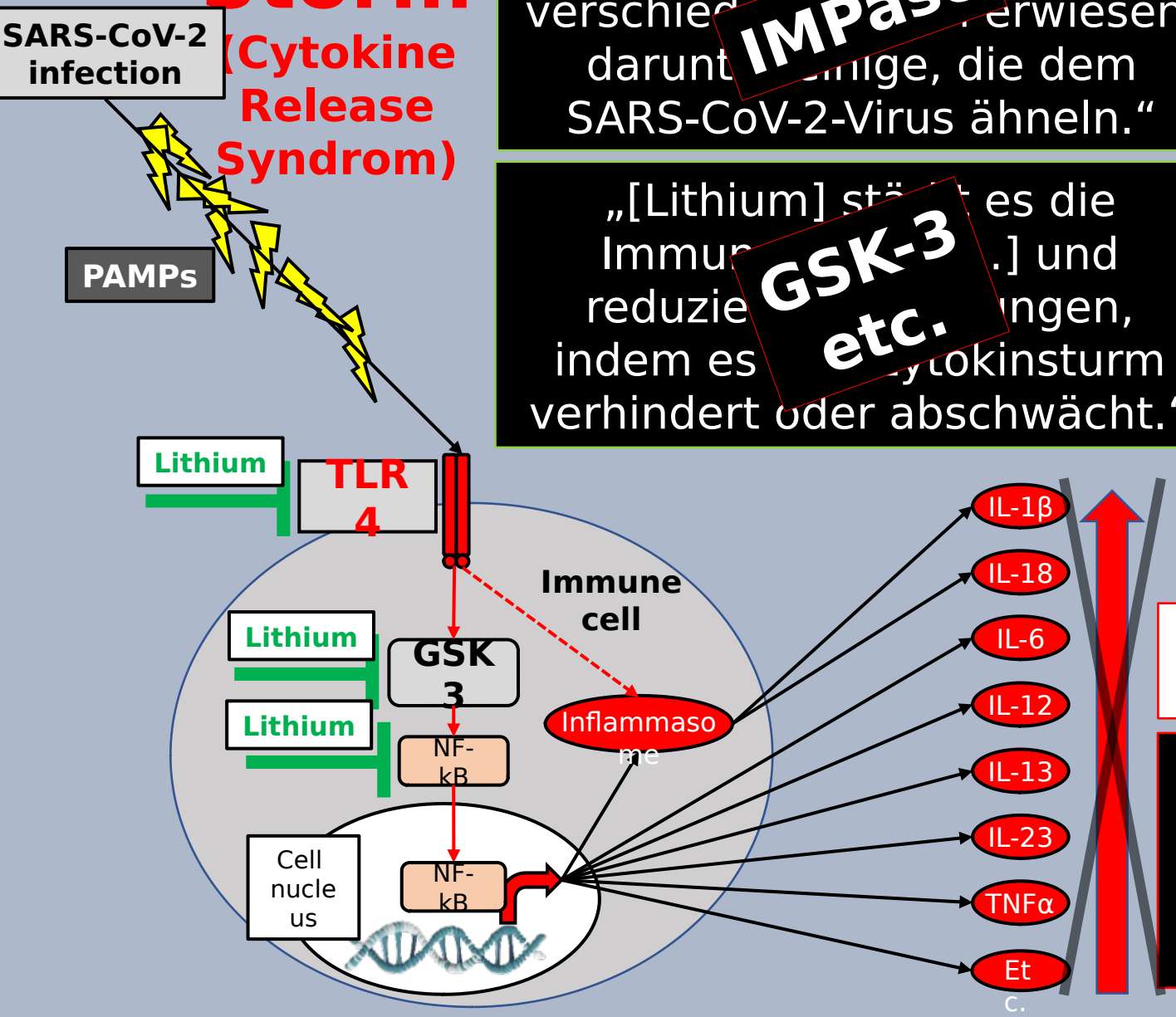
[a] UGC de Neumología, Instituto Maimónides de Investigación Biomédica de Córdoba 9 (IMIBIC). Hospital Universitario Reina Sofía, Universidad de Córdoba, Avda. Menéndez 10 Pidal s/n, 14004 11, Córdoba, Spain
[b] Departamento de Medicina Interna. IMIBIC, CIBER de Fisiopatología de la Obesidad y la Nutrición. Hospital Universitario Reina Sofía, Universidad de Córdoba, Fundación Progreso y Salud. Avda. Menéndez Pidal s/n, 14004 14, Córdoba, Spain
[c] Department of Chronic Diseases, Metabolism and Ageing, Laboratory of Clinical and Experimental Endocrinology, KU Leuven, Herestraat, ON1/902, 3000, Leuven, Belgium
[d] IMIBIC. CIBER de Fragilidad y Envejecimiento Saludable. Hospital Universitario Reina Sofía, Universidad de Córdoba, Fundación Progreso y Salud. Avda. Menéndez Pidal s/n, 18 14004, Córdoba, Spain

Vit D deficiency **causes** severe COVID-19!

examples show that the cytokine storm in COVID-19 results from inflammation, rather than from the virus itself. This information is critical when it comes to the selection of the treatments.

„[…] der Zytokinsturm bei schweren COVID-19-Verläufen resultiert eher aus der Entzündung, als aus dem Virus selbst. Diese Information ist entscheidend für die Auswahl der Behandlungsmethode."

Cytokine Storm (Cytokine Release Syndrom)



„Lithium hat sich als wirksam gegen die V… hrung verschied… erwiesen, darunt… ige, die dem SARS-CoV-2-Virus ähneln.“

IMPase

„[Lithium] st… es die Immun… .] und reduzie… ngen, indem es …tokinsturm verhindert oder abschwächt.“

GSK-3 etc.

frontiers in Pharmacology

CASE REPORT
published: 27 August 2020
doi: 10.3389/fphar.2020.557629

August 27, 2020

Does Lithium Deserve a Place in the Treatment Against COVID-19? A Preliminary Observational Study in Six Patients, Case Report

Carlos Spuch[1†], Marta López-García[2†], Tania Rivera-Baltanás[1], Daniela Rodrígues-Amorím[1] and José M. Olivares[3,4]*

[1] Translational Neuroscience Research Group, Galicia Sur Health Research Institute (IISGS), CIBERSAM, Vigo, Spain, [2] Department of Psychiatry, Hospital Álvaro Cunqueiro, Translational Neuroscience Research Group, Galicia Sur Health Research Institute (IISGS), CIBERSAM, Vigo, Spain, [3] Department of Psychiatry, Hospital Álvaro Cunqueiro, Vigo, Spain, [4] Neuroscience Research Area, Galicia Sur Health Research Institute (IISGS), CIBERSAM, Vigo, Spain

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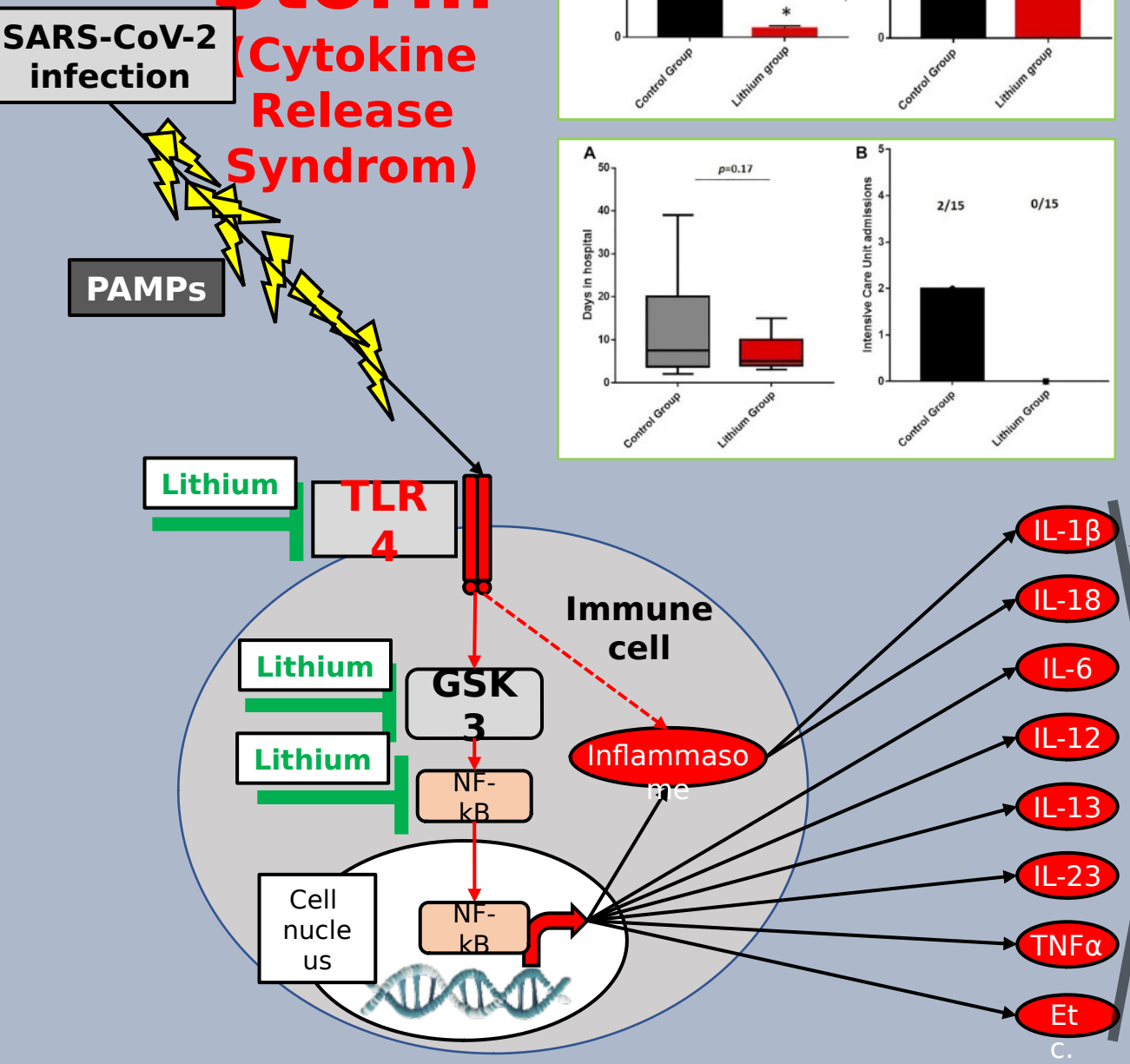
Niklas Beyersdorf, Julius Maximilian University of Würzburg, Germany

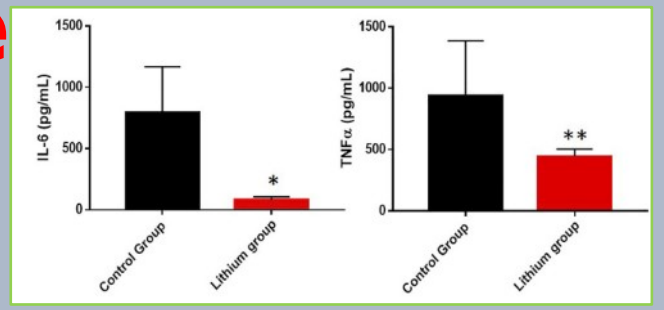
Lithium has shown the capacity to: a) inhibit the replication of several types of viruses, some of which are similar to the SARS-CoV-2 virus, b) increase the immune response by reducing lymphopenia, and c) reduce inflammation by preventing or reducing the cytokine storm. In the present study, we have treated six patients with severe COVID-19 infection with lithium carbonate. We found that lithium carbonate significantly reduced plasma reactive C-Protein levels, increased lymphocyte numbers and decreased the neutrophil-lymphocyte ratio, improving both inflammatory activity and the immune response in these patients. We propose that lithium carbonate may deserve a place in the treatment against COVID-19.

examples show that the cytokine storm in COVID-19 results from inflammation, rather than from the virus itself. This information is critical when it comes to the selection of the treatments.

„[…] der Zytokinsturm bei schweren COVID-19-Verläufen resultiert eher aus der Entzündung, als aus dem Virus selbst. Diese Information ist entscheidend für die Auswahl der Behandlungsmethode.“

Cytokine Storm (Cytokine Release Syndrom)





frontiers | Frontiers in Pharmacology
ORIGINAL RESEARCH
published: 14 April 2022
doi: 10.3389/fphar.2022.850583

April 14, 2022

Efficacy and Safety of Lithium Treatment in SARS-CoV-2 Infected Patients

OPEN ACCESS

Edited by:
Olumayokun Olajide,
University of Huddersfield,
United Kingdom

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Lithium treatment stops severe COVID-19!

examples show that the cytokine storm in COVID-19 results from inflammation, rather than from the virus itself. This information is critical when it comes to the selection of the treatments.

„[…] der Zytokinsturm bei schweren COVID-19-Verläufen resultiert eher aus der Entzündung, als aus dem Virus selbst. Diese Information ist entscheidend für die Auswahl der Behandlungsmethode.“

CONCLUSION

This randomized clinical trial demonstrates that lithium carbonate treatment is safe and effective in curbing the severity caused by SARS-CoV-2 infection. SARS-CoV-2 infection induces exaggerated inflammation driven by components of innate immunity. We demonstrated that lithium was able to reduce the number of days of hospital and ICU admission as well as the risk of death. Lithium, through its immunomodulatory action, reduces inflammatory cytokine levels by preventing cytokine storms, thus reducing the severity of the infection and the risk of death. In fact, lithium can also be studied for earlier use, such as at the time of diagnosis, in order to avoid hospitalization altogether, as well as in the treatment of "Long Covid" syndromes. From the "Big Bang" to its presence in all living things, to its use in medicine, and in the storage of electricity, the third element of the Periodic Table may be paramount in life, which cannot be spelled without Li.

„Lithium senkt den Spiegel entzündungsfördernder Zytokine und verhindert somit Zytokinstürme. Dadurch verringert sich der Schweregrad der Infektion und das

frontiers | Frontiers in Pharmacology

ORIGINAL RESEARCH
published: 14 April 2022
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April 14, 2022

Efficacy and Safety of Lithium Treatment in SARS-CoV-2 Infected Patients

OPEN ACCESS

Edited by:
Olumayokun Olajide,
University of Huddersfield,
United Kingdom

Carlos Spuch[1*†], Marta López-García[1,2†], Tania Rivera-Baltanás[1†], J. J Cabrera-Alvargonzález[3], Sudhir Gadh[4], Daniela Rodrigues-Amorim[1,5], Tania Álvarez-Estévez[1,2], Almudena Mora[1], Marta Iglesias-Martínez-Almeida[1,6], Luis Freiría-Martínez[1,6], Maite Pérez-Rodríguez[7], Alexandre Pérez-González[7], Ana López-Domínguez[7], María Rebeca Longueira-Suarez[7], Adrián Sousa-Domínguez[7], Alejandro Araújo-Ameijeiras[7], David Mosquera-Rodríguez[1,8], Manuel Crespo[3], Dolores Vila-Fernández[8], Benito Regueiro[3,9,10] and Jose Manuel Olivares[1,2]

„Tatsächlich kann Lithium auch zu einem früheren Zeitpunkt eingesetzt werden, beispielsweise zum Zeitpunkt der Diagnose, um einen Krankenhaus-aufenthalt gänzlich zu vermeiden, sowie bei der Behandlung von ´Long-COVID'-Syndromen."

„Vom ´Urknall´ über sein Vorkommen in allen Lebewesen […] ist das dritte Element des Periodensystems das vielleicht wichtigste Element im Leben (in ´*Life*´), das ohne *Li* nicht buchstabiert werden kann."

Causal Chain Lithium Deficienc

SARS-CoV-2 infection / Spike-mRNA injection

creased stress reaction
nder psychologic strain

increased neurotoxic Cortisol release

DAMPs

PAMPs

Lithium

Lithium

TLR 4

Vicious Cycle of Neuro-inflammation

Zytosol/ Zytoplasma

Lithium

GSK 3

Lithium

NF-kB

Inflammaso m

NF-kB

Microglia Immune cell of the brain

Cell nucleus

IL-1β

IL-18

IL-6

IL-12

IL-13

IL-23

TNFα

Et

Lithium

e.g. BDNF Neurogenese

adult hippocampal neurogenesis & mental immune system

hippocampal loss of function and volume

Lithium

nti-
poptose

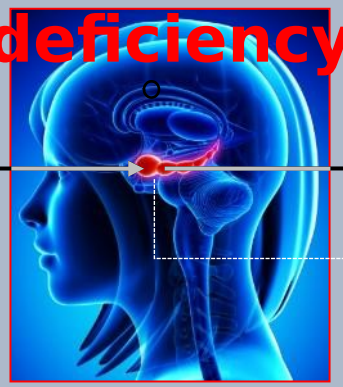
hippocampal development disturbanc

neuropsychiatric development disorders (schizophrenia, bipolar, etc)

chronic fatigue spikeopathy (brain fog) depression Alzheimer's

Lithium deficiency

reduced psychological resilience ... „sickness behavior“



Hippocampus
Center of mental immune system

SARS-CoV-2 infection / Spike-mRNA injection

educed stress reaction
nder psychologic strain

increased experience

PAMPs

Lithium

Lithium

TLR 4

Zytosol/ Zytoplasma

Lithium

GSK 3

Lithium

NF-kB

Inflammaso m

IL-1β

IL-18

IL-6

IL-12

IL-13

IL-23

TNFα

Et

Microglia
Immune cell of the brain

Cell nucleus

NF-kB

adult hippocampal neurogenesis & mental immun system

Virtuous cycle of mental growth

increased psychological resilience
...
„mental health“

Hippocampus
Center of mental immune systems

Shorter and unhealthier life

Lithium deficiency

Chronic fatique, depression, etc.

Zytokine storm risk: traumata,

arterioscleros

Polyneuropathy, migraines, etc.

Neurodegeneration: ALS, Alzheimer's, Parkinson's, etc.

Gigantic drug market

chronically healthy

Longer and healthier life

Lithium sufficiency

Activates nerve cell production and growth

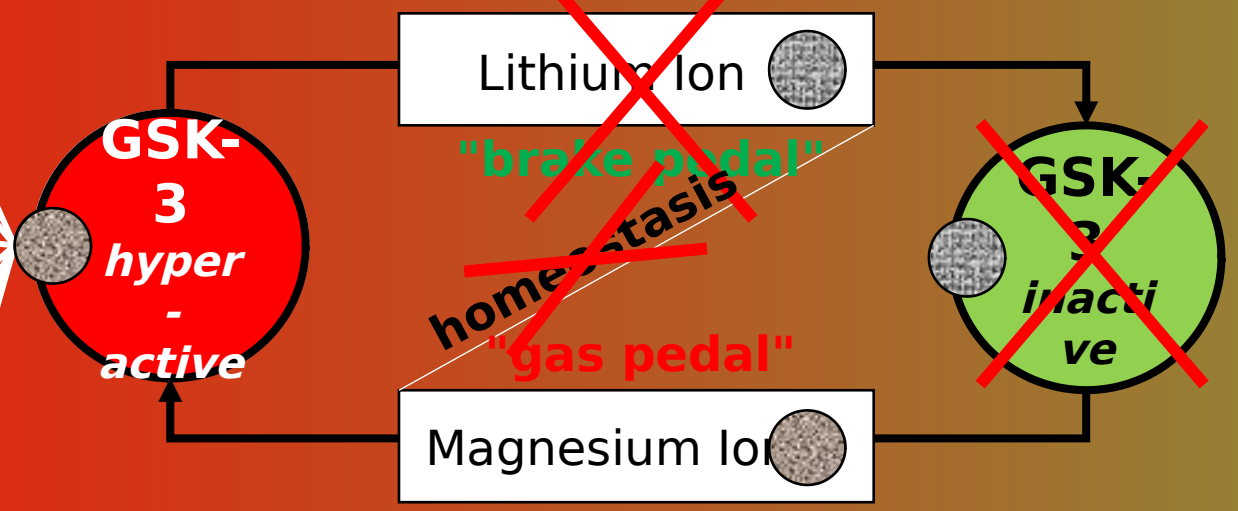
Promotes mental development and

mass

Improves blood sugar and blood pressure regulation

Promote lithium deficiency

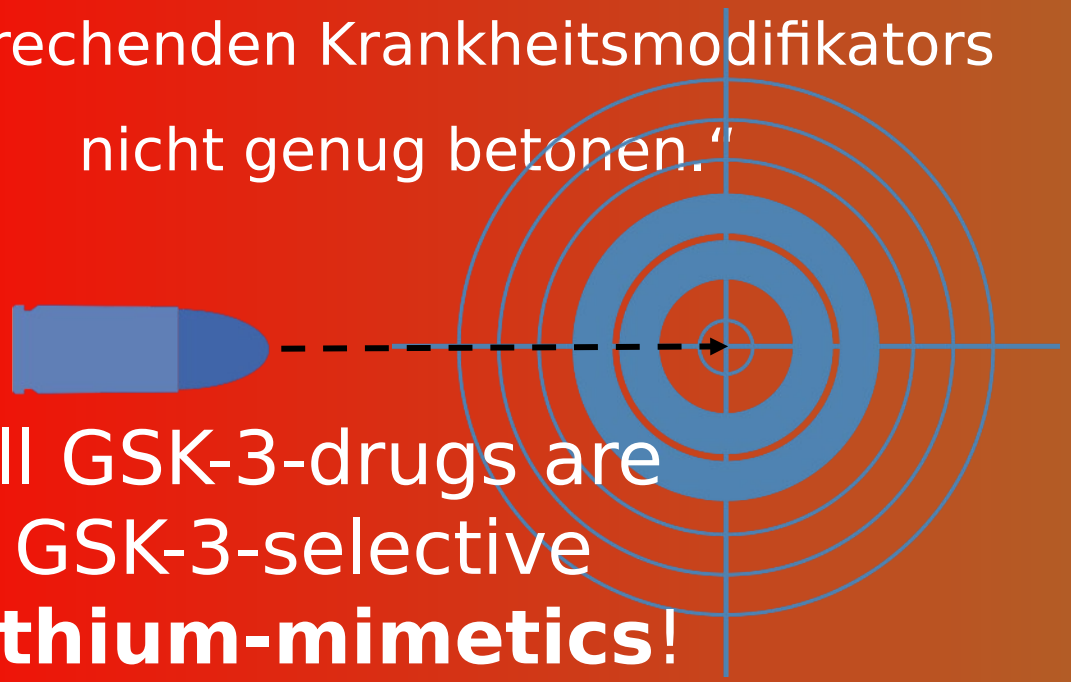
homeostasis (self-regulation)



Both trace elements are essential!

yperactive Lithium Target GSK-

„Seit seiner ersten Entdeckung im Jahr 1980 und den darauffolgenden Jahrzehnten der Forschung kann man die Bedeutung des **Targets** und das Versprechen eines bahnbrechenden Krankheitsmodifikators nicht genug betonen.“



All GSK-3-drugs are GSK-3-selective **lithium-mimetics**!

Sage Journals

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Journal of Alzheimer's Disease

IOS Press

Impact Factor: 3.4

Restricted access | Review article | First published online May 11, 2018

2018

The Conundrum of GSK3 Inhibitors: Is it the Dawn of a New Beginning?

Ratan V. Bhat, Ulf Andersson, [...], and Anna K. Sundgren-Andersson +3 View all authors and affiliations

Volume 64, Issue s1 | https://doi.org/10.3233/JAD-179934

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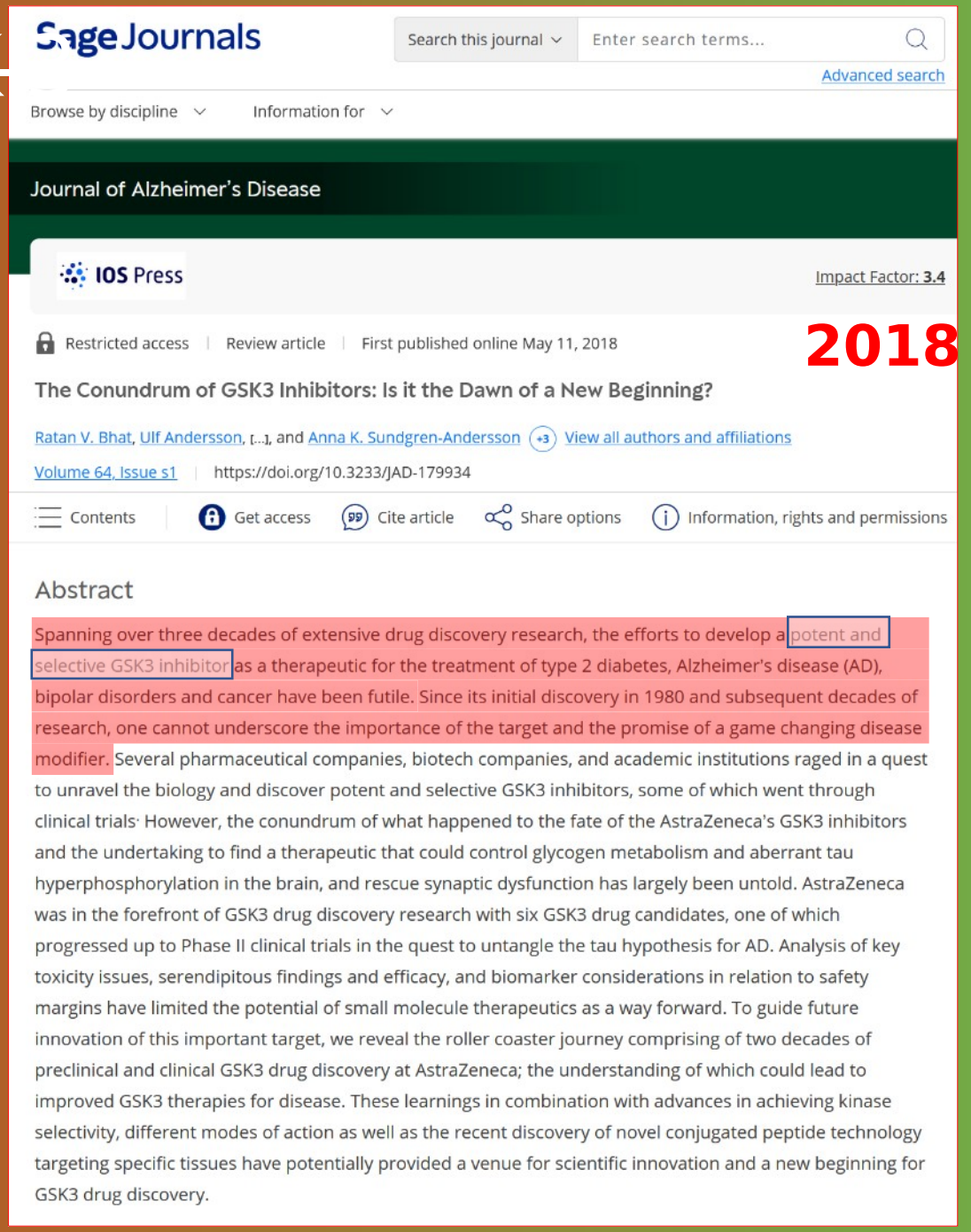
Abstract

Spanning over three decades of extensive drug discovery research, the efforts to develop a potent and selective GSK3 inhibitor as a therapeutic for the treatment of type 2 diabetes, Alzheimer's disease (AD), bipolar disorders and cancer have been futile. Since its initial discovery in 1980 and subsequent decades of research, one cannot underscore the importance of the target and the promise of a game changing disease modifier. Several pharmaceutical companies, biotech companies, and academic institutions raged in a quest to unravel the biology and discover potent and selective GSK3 inhibitors, some of which went through clinical trials· However, the conundrum of what happened to the fate of the AstraZeneca's GSK3 inhibitors and the undertaking to find a therapeutic that could control glycogen metabolism and aberrant tau hyperphosphorylation in the brain, and rescue synaptic dysfunction has largely been untold. AstraZeneca was in the forefront of GSK3 drug discovery research with six GSK3 drug candidates, one of which progressed up to Phase II clinical trials in the quest to untangle the tau hypothesis for AD. Analysis of key toxicity issues, serendipitous findings and efficacy, and biomarker considerations in relation to safety margins have limited the potential of small molecule therapeutics as a way forward. To guide future innovation of this important target, we reveal the roller coaster journey comprising of two decades of preclinical and clinical GSK3 drug discovery at AstraZeneca; the understanding of which could lead to improved GSK3 therapies for disease. These learnings in combination with advances in achieving kinase selectivity, different modes of action as well as the recent discovery of novel conjugated peptide technology targeting specific tissues have potentially provided a venue for scientific innovation and a new beginning for GSK3 drug discovery.

yperactive Lithium Target GSK-

„Seit seiner ersten Entdeckung im Jahr 1980 und den darauffolgenden Jahrzehnten der Forschung kann man die Bedeutung des **Targets** und das Versprechen eines bahnbrechenden Krankheitsmodifikators nicht genug betonen.“

„Über drei Jahrzehnte intensiver Forschung im Bereich der Arzneimittelentdeckung hinweg waren die Bemühungen, einen potenten und selektiven GSK3-Hemmer als Therapeutikum zur Behandlung von Typ-2-Diabetes, Alzheimer, bipolaren Störungen und Krebs zu entwickeln, **vergeblich**.“



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Nehls *Journal of Molecular Psychiatry* (2016) 4:3
DOI 10.1186/s40303-016-0018-8

Journal of Molecular Psychiatry

July 15, 2016

REVIEW Open Access

Unified theory of Alzheimer's disease (UTAD): implications for prevention and curative therapy

Michael Nehls

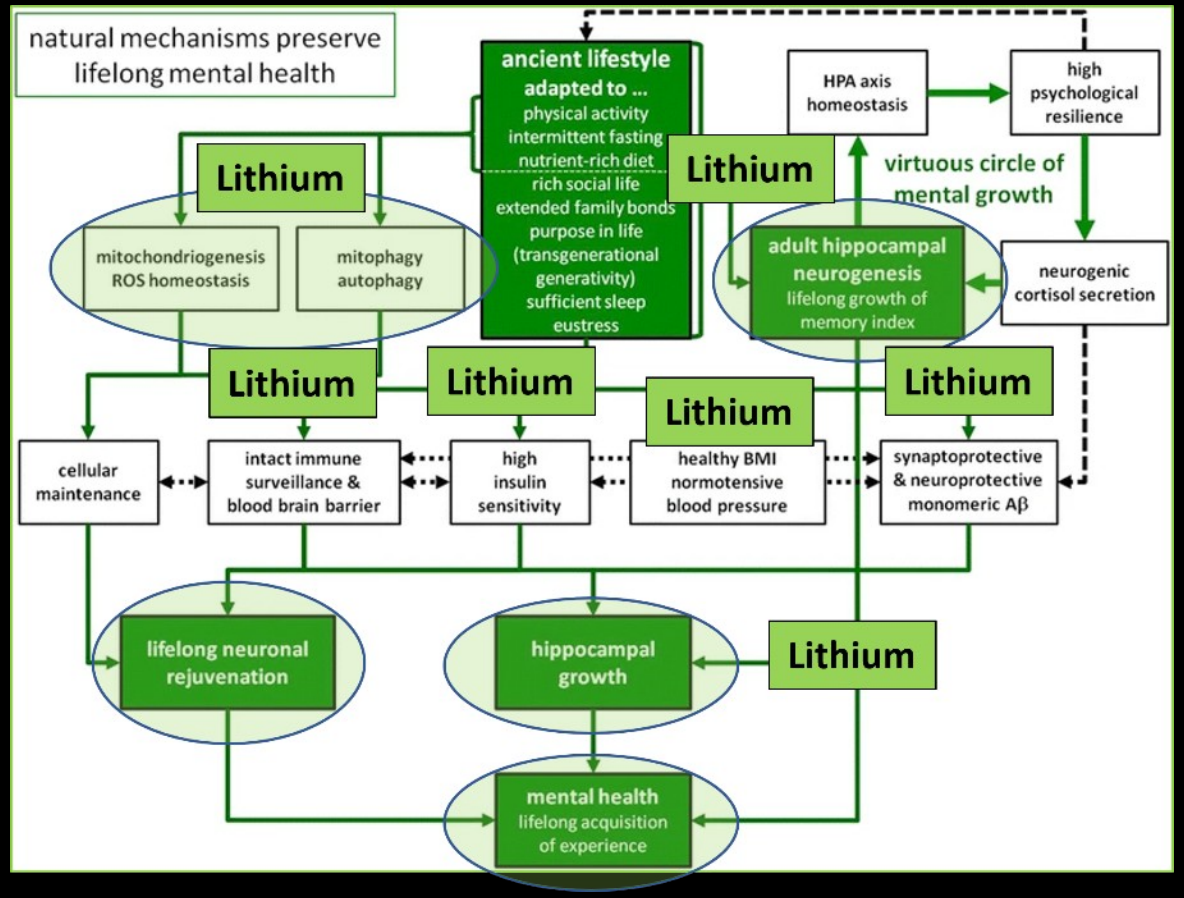
frontiers Frontiers in Pharmacology

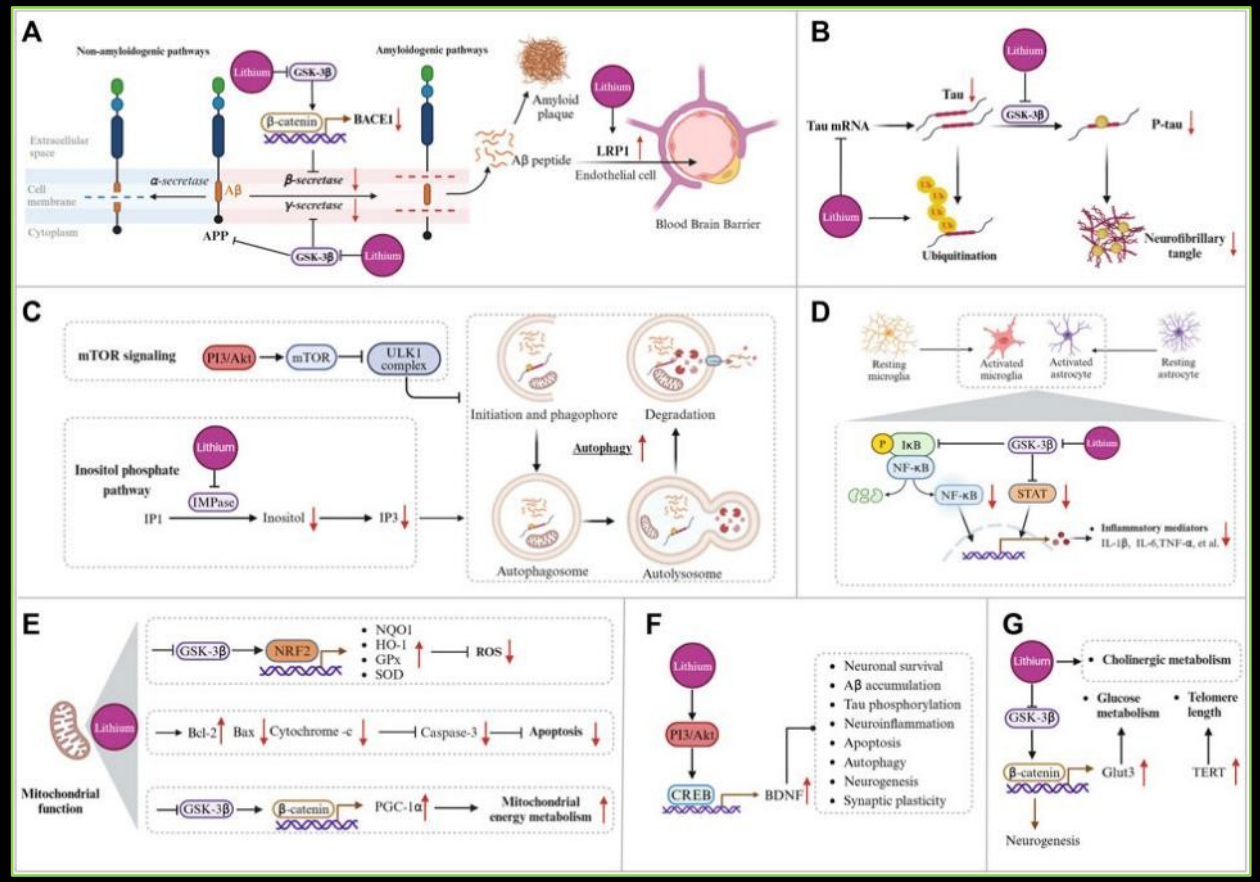
July 11, 2024

Molekulare Mechanismen und therapeutisches Potenzial von Lithium bei Alzheimer: Umwidmung einer alten Wirkstoffklasse

Molecular mechanisms and therapeutic potential of lithium in Alzheimer's disease: repurposing an old class of drugs

Yanxin Shen[1,2], Meng Zhao[1,2], Panpan Zhao[1,2], Lingjie Meng[1,2], Yan Zhang[1,2], Guimei Zhang[1,2], Yezi Taishi[3] and Li Sun[1,2]*





pharmaceuticals

April 5, 2025

MDPI

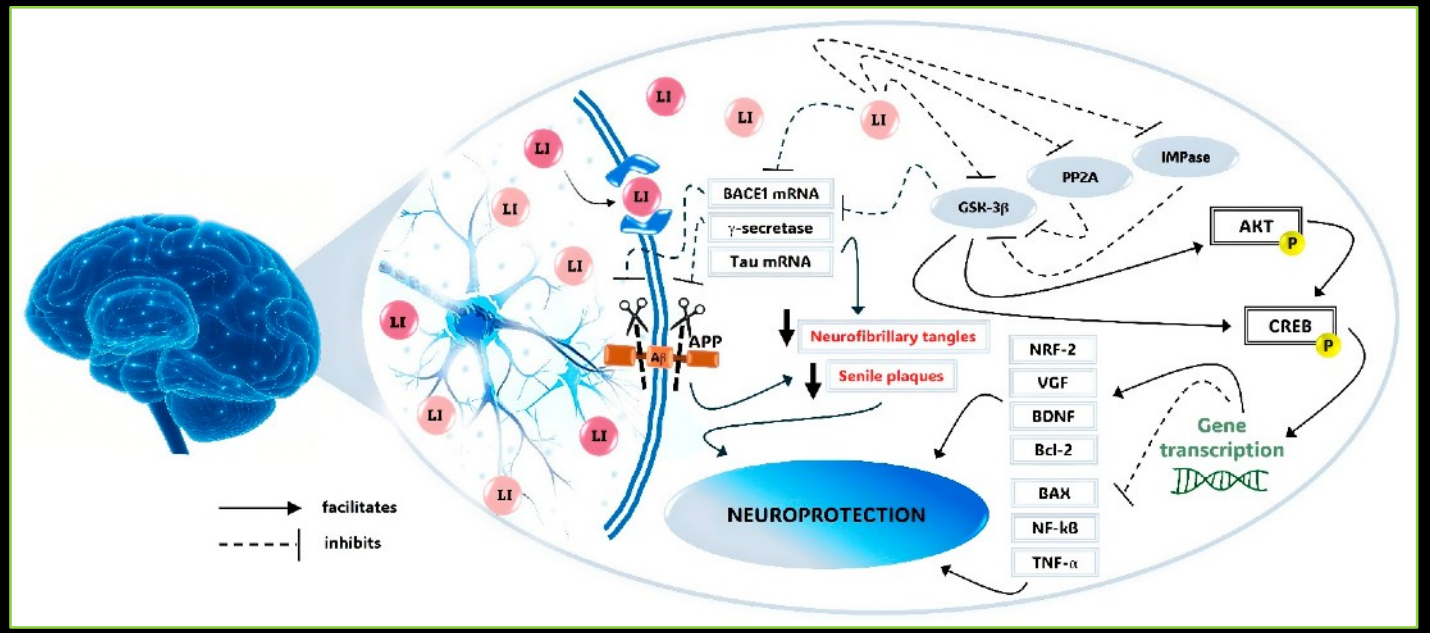
Review

An Overview of the Effects of Lithium on Alzheimer's Disease: A Historical Perspective

Marcia Radanovic [1,2,†], Monique Patricio Singulani [1,2,3,†], Vanessa de Jesus R. De Paula [1,2], Leda Leme Talib [1,2] and Orestes Vicente Forlenza [1,2,3,*]

[1] Laboratory of Neuroscience (LIM-27), Department and Institute of Psychiatry, Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo (HCFMUSP), São Paulo 05403-010, SP, Brazil; marciaradanovic@gmail.com (M.R.); moniquesingulani@gmail.com (M.P.S.); vanessajrpaula@gmail.com (V.d.J.R.D.P.); ledatalib@gmail.com (L.L.T.)
[2] Instituto Nacional de Biomarcadores em Neuropsiquiatria (INBioN), Conselho Nacional de Desenvolvimento Científico e Tecnológico, São Paulo 05403-010, SP, Brazil
[3] Centro de Neurociências Translacionais (CNT), Faculdade de Medicina da Universidade de São Paulo (FMUSP), São Paulo 05403-010, SP, Brazil
* Correspondence: forlenza@usp.br
† These authors contributed equally to this work.

„These findings suggest that the intake of lithium in low



Neurobiological properties of lithium

- Preventing protein misfolding
- Neuroprotective effects
- Antiapoptotic effects
- Reducing oxidative stress
- Inducing neuroplasticity
- Modulating neurotransmitters
- Reducing neuroinflammation
- Preventing mitochondrial dysfunction
- Neurotrophic effects
- Inducing autophagy

ium Acts on All (!) Lithium Targets *Simultaneou*
essential amounts are sufficient for health effec

January 2013

Current Alzheimer Research, 2013, *10*, 0000-0000 1

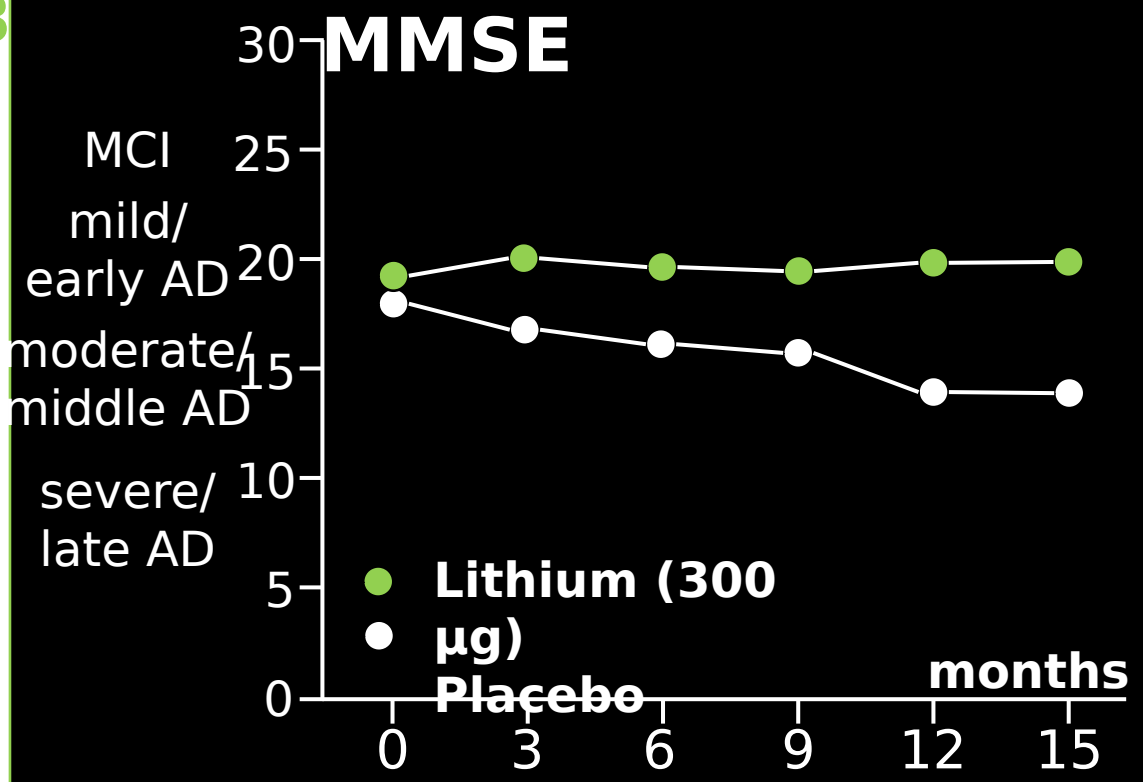
Microdose Lithium Treatment Stabilized Cognitive Impairment in Patients with Alzheimer's Disease

Marielza Andrade Nunes[1], Tania Araujo Viel[2] and Hudson Sousa Buck[1,*]

[1]*Department of Physiological Sciences, Faculdade de Ciencias Medicas da Santa Casa de Sao Paulo. R. Dr. Cesario Motta Jr, 61, CEP: 01221-020, Sao Paulo, SP, Brazil;* [2]*Laboratory of Neuropharmacology and Aging, School of Arts, Sciences and Humanities, Universidade de Sao Paulo. Av. Arlindo Bettio, 1000, CEP: 03828-000, São Paulo, SP, Brazil*

Abstract: A lower incidence of dementia in bipolar patients treated with lithium has been described. This metal inhibits the phosphorylation of glycogen-synthase-kinase 3-α and β, which are related to amyloid precursor protein processing and tau hyperphosphorylation in pathological conditions, respectively. Following the same rationale, a group just found that lithium has disease-modifying properties in amnestic mild cognitive impairment with potential clinical implications for the prevention of Alzheimer's Disease (AD) when a dose ranging from 150 to 600 mg is used. As lithium is highly toxic in regular doses, our group evaluated the effect of a microdose of 300µg, administered once daily on AD patients for 15 months. In the evaluation phase, the treated group showed no decreased performance in the mini-mental state examination test, in opposition to the lower scores observed for the control group during the treatment, with significant differences starting three months after the beginning of the treatment, and increasing progressively. This data suggests the efficacy of a microdose lithium treatment in preventing cognitive loss, reinforcing its therapeutic potential to treat AD using very low doses.

Keywords: Alzheimer, lithium, GSK-3, Tau, aging, memory.



l studies prove the causal relationship between lithium defic
and the correlations observed in epidemiological studies.

Nehls J… of Molecular Psychiatry (2016) 4:3
DOI 10.1186/… 016-0018-8

July 15, 2016

REVIEW

Unified theory of Alzheimer's disease (UTAD): implications for prevention and curative therapy

Michael Nehls

2024

mechanisms and
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Zhao[1,2], Panpan Zhao[1,2], Lingjie Meng[1,2],
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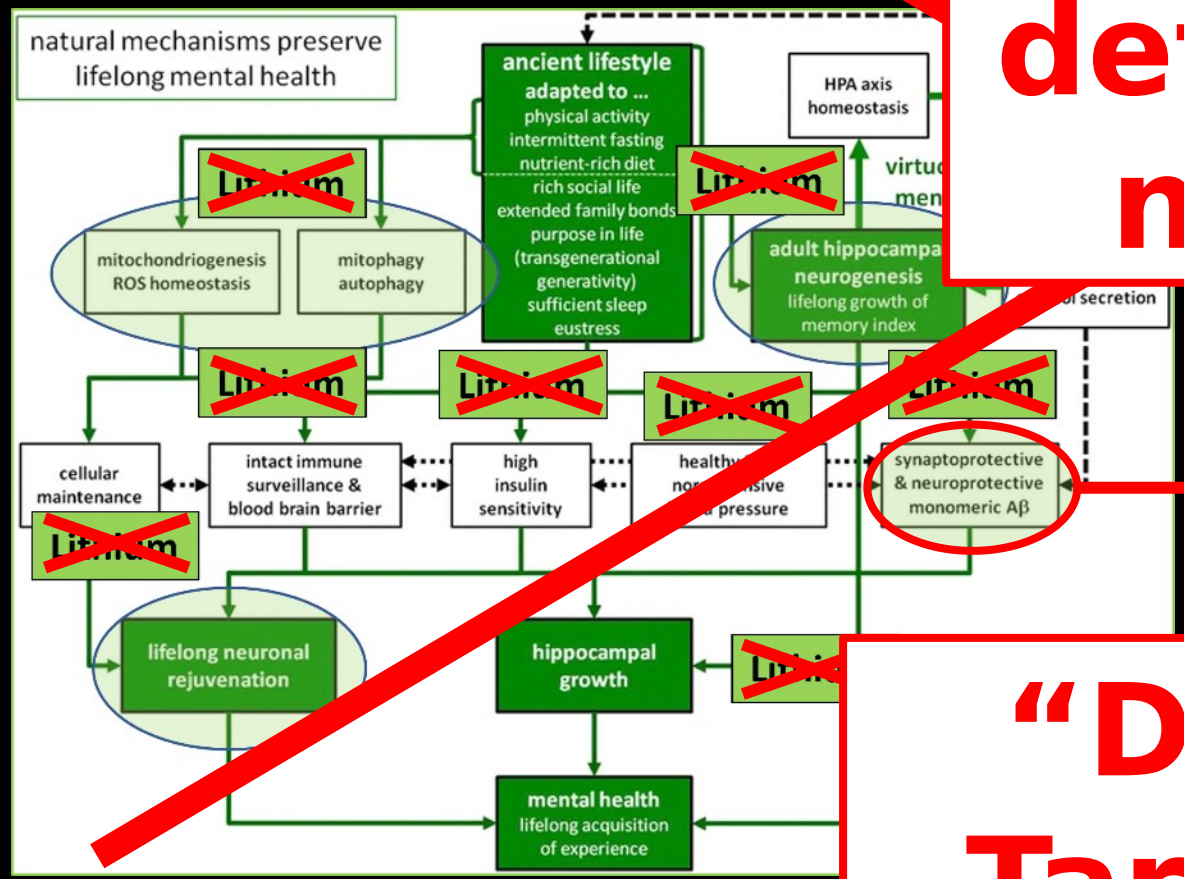
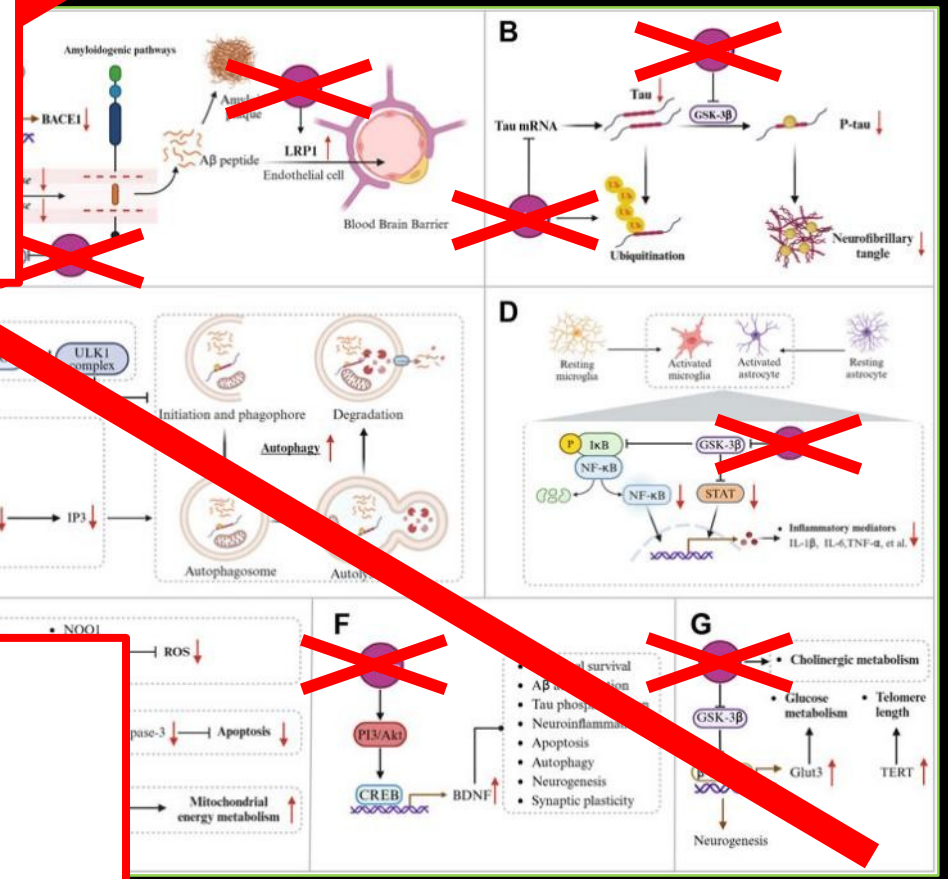
Molekulare Mechanismen und therapeutisches Potenzial von Lithium bei Alzheimer: Umwidmung einer alten Wirkstoffklasse

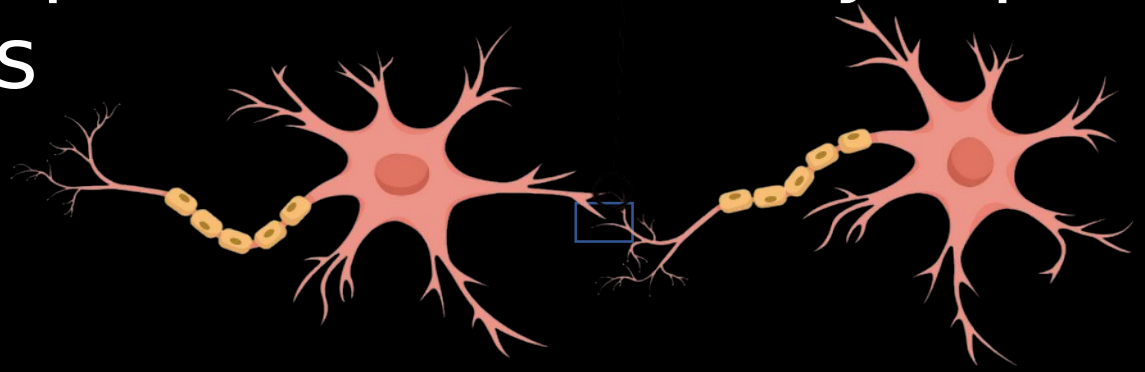
Promote lithium deficiency





"Drug-Target"

β-Amyloid (Aβ) – Essential for Synaptic Function and Homeostasis



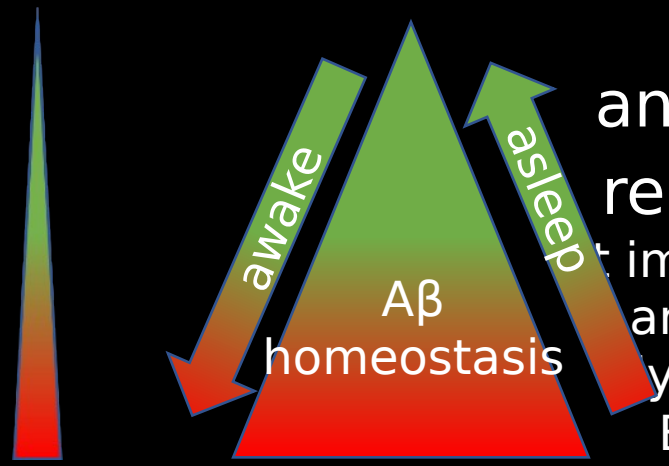
synaptic Aβ-concentration

hippocampal Aβ-concentration

Synapse ***open*** for new information

Synapse ***activity*** leads to Aβ release

Synapse ***closed*** for new



Aβ clearance and homeostasis are regulated by lithium

t improves circadian rhythm and deep sleep, activates ymphatic system and the BBB pump mechanism.

Brain Behav Immun. 2018 May;70:36-47. doi: 10.1016/j.bbi.2018.03.007. Epub 2018 Mar 12.

Cognitive benefits of lithium chloride in APP/PS1 mice are associated with enhanced brain clearance of β-amyloid

Yijun Pan [1], Jennifer L Short [2], Stephanie A Newman [1], Kwok H C Choy [2], Durgesh Tiwari [2], Christopher Yap [1], Danielle Senyschyn [1], William A Banks [3], Joseph A Nicolazzo [4]

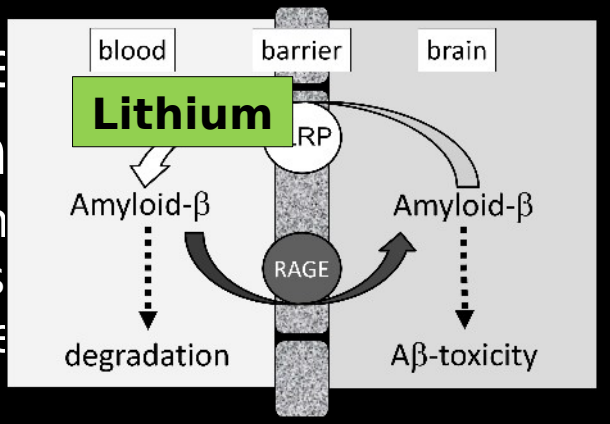
Affiliations – collapse

Affiliations

1 Drug Delivery, Disposition and Dynamics, Monash Institute of Pharmaceutical Sciences, Monash University, Parkville, Victoria, Australia.
2 Drug Discovery Biology, Monash Institute of Pharmaceutical Sciences, Monash University, Parkville, Victoria, Australia.
3 Geriatric Research Education and Clinical Center, Veterans Affairs Puget Sound Health Care System, Seattle, WA, USA; Division of Gerontology and Geriatric Medicine, Department of Medicine, University of Washington School of Medicine, Seattle, WA, USA.
4 Drug Delivery, Disposition and Dynamics, Monash Institute of Pharmaceutical Sciences, Monash University, Parkville, Victoria, Australia. Electronic address: joseph.nicolazzo@monash.edu.

2018

PMID: 29545118 DOI: 10.1016/j.bbi.2018.03.007



β-Amyloid (Aβ) was defined as the only acceptable target for pharmaceutical drug development—i.e., vaccination!

tps://de.freep

OPINION
GUEST ESSAY

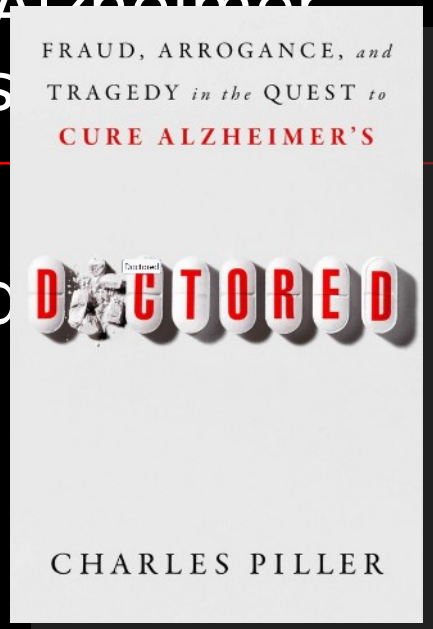
The Devastating Legacy of Lies in Alzheimer's Science

U.S. INTERNATIONAL CANADA ESPAÑOL 中文
The New York Times

Das verheerende Erbe der Lügen in der Alzheimer-Forschung

Jan. 24, 2025

β-Amyloid-dogma



https://www.nytimes.com/2025/01/24/

**For decades, Alzheimer's research has been shaped by the dominance of a single theory,
the amyloid hypothesis. […] The supremacy of that hypothesis has exerted enormous pressure toward scientific conformity.**

**Seit Jahrzehnten wird die Alzheimer-Forschung von einer einzigen Theorie dominiert:
der Amyloid-Hypothese. Die Vorherrschaft dieser Hypothese hat**

Nearly every drug approved for Alzheimer's dementia symptoms is based on it, despite producing meager results.

**Fast jedes für die Symptome der Alzheimer-Demenz zugelassene Medikament basiert darauf,
obwohl sie nur magere Ergebnisse erzielen.**

The drugs are also not benign, posing risks of death or serious brain injury, and they can shrink the brain faster than Alzheimer's itself.

**Zudem sind die Medikamente nicht harmlos, sondern bergen das Risiko von Todesfällen oder schweren
Hirnschädigungen und können das Gehirn schneller schrumpfen lassen als die**

The entrenchment of the amyloid hypothesis has fostered a kind of groupthink where grants, corporate riches, career advancement and professional reputations often depend on a central idea largely accepted by institutional authorities on faith.

Die Verfestigung der Amyloid-Hypothese hat eine Art Gruppendenken gefördert, bei dem Fördermittel, Unternehmensgewinne, beruflicher Aufstieg und der Ruf von Fachleuten oft von einer zentralen Idee abhängen, die von

It's unsurprising, then, that most of the fraudulent or questionable papers uncovered during my reporting have involved aspects of the amyloid hypothesis.

Es ist daher nicht verwunderlich, dass die meisten der während meiner Recherchen aufgedeckten betrügerischen oder fragwürdigen

FDA's Decision to Approve New Treatment for Alzheimer's Disease

June 7, 2021

U.S. FOOD & DRUG ADMINISTRATION

By Dr. Patrizia Cavazzoni, Director, FDA Center for Drug Evaluation and Research

Today FDA approved Aduhelm (aducanumab) to treat patients with Alzheimer's disease using the Accelerated Approval pathway, under which the FDA approves a drug for a serious or life-threatening illness that may provide meaningful therapeutic benefit over existing treatments when the drug is shown to have an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit to patients and there remains some uncertainty about the drug's clinical benefit.

„Die FDA genehmigt ein Medikament für eine schwere oder lebensbedrohliche Erkrankung, wenn es gegenüber bestehenden Behandlungen einen bedeutenden therapeutischen Nutzen bieten kann und eine Wirkung auf einen Surrogatendpunkt zeigt, der mit hinreichender Wahrscheinlichkeit einen klinischen Nutzen für Patienten vorhersagt. Dies gilt jedoch nur, wenn hinsichtlich des klinischen Nutzens

https://www.fda.gov/drugs/our-perspective/fdas-decision-approve-new-treatment-alzheimers-

RESEARCH ARTICLE

May 16, 2023

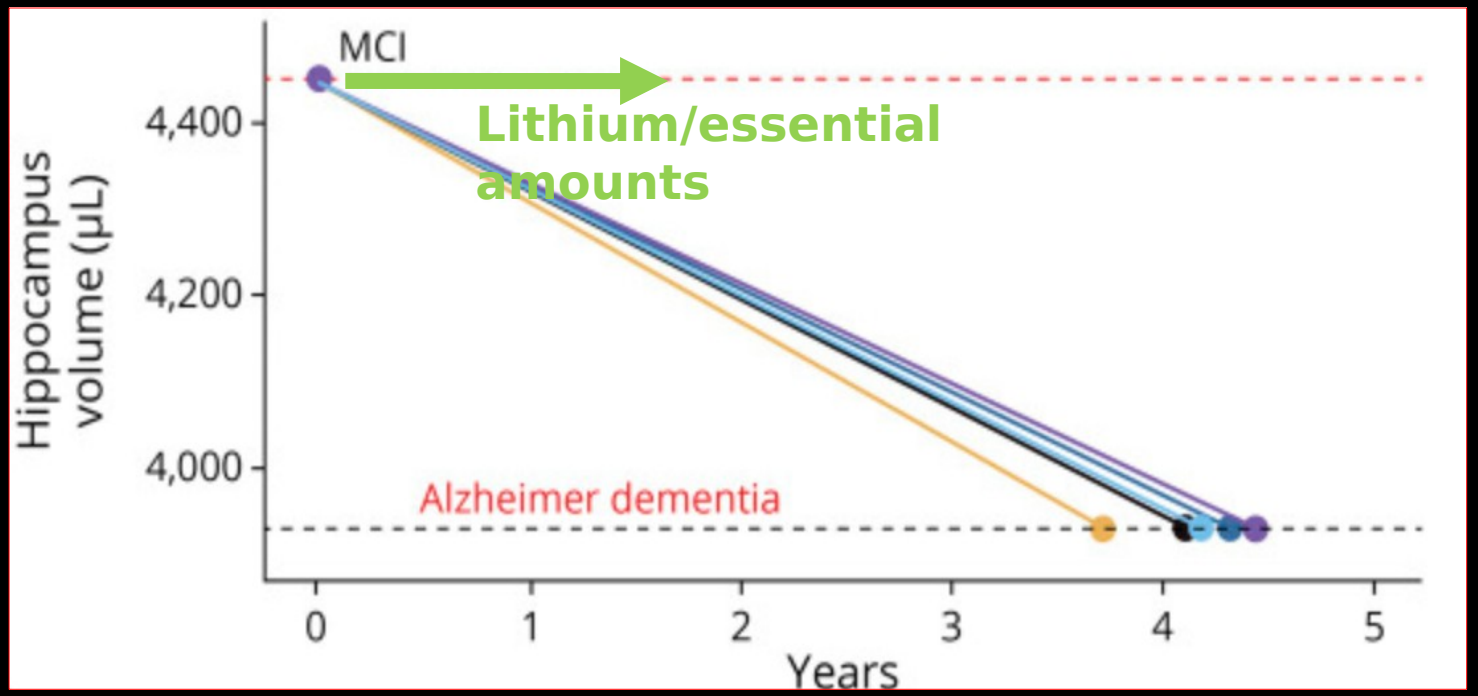
Accelerated Brain Volume Loss Caused by Anti–β-Amyloid Drugs

A Systematic Review and Meta-analysis

Francesca Alves, BBMED(Hons), PhD, Pawel Kalinowski, BBSc(Hons), MBiostat, PhD, and Scott Ayton, PhD

Neurology® 2023;100:e2114-e2124. doi:10.1212/WNL.0000000000207156

Recommendation #1: "Clinicians who prescribe […] **anti-Aβ monoclonal antibodies** should inform current and new patients that these drugs have been shown to **accelerate markers of** **odegeneration** […]."



Placebo

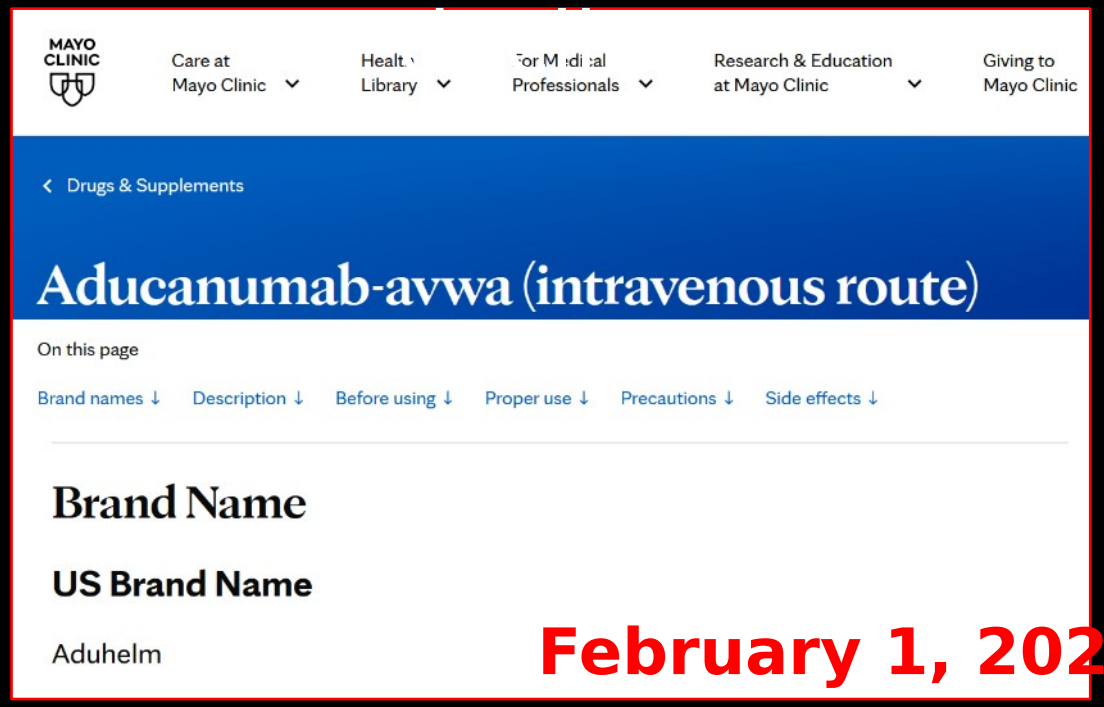
Monoclonal antibodies

Secretase-inhibitor

ll „therapeutics"

https://pubmed.ncbi.nlm.nih.gov/36973044/

Accelerated Approval – accelerated mental



February 1, 2025

„Falsche Überzeugungen können nicht durch Fakten geändert werden “

Side Effects

Along with its needed effects, a medicine may cause some unwanted effects. Although not all of these side effects may occur, if they do occur they may need medical attention.

Check with your doctor or nurse immediately if any of the following side effects occur:

More common

- Blurred or changes in vision
- Confusion
- Confusion as to time, place, or person
- Dizziness
- Falls
- Hallucinations
- Headache
- Holding false beliefs that cannot be changed by fact
- Mental depression or anxiety
- Nausea
- Nightmares or unusually vivid dreams
- Problems with movement, walking, or speech
- Seizures
- Sleepiness or unusual drowsiness
- Unusual excitement, nervousness, or restlessness
- Vomiting

www.mayoclinic.org/drugs-supplements/aducanumab-avwa-intravenous-route/description/drg-20516708

November, 2022
Ageing Research Reviews
Volume 81, November 2022, 101709

Review

Comparative efficacy of lithium and aducanumab for cognitive decline in patients with mild cognitive impairment or Alzheimer's disease: A systematic review and network meta-analysis

Itsuki Terao, Mina Honyashiki, Takeshi Inoue

November, 2022

Background: In 2021, the US Food and Drug Administration granted an accelerated approval to aducanumab for patients with mild cognitive impairment (MCI) and mild dementia caused by Alzheimer's disease (AD); however, the cost of aducanumab is high, at approximately $28,000 for one year per person. On the other hand, lithium is much cheaper at $40 a year, and has been reported to be effective for the cognitive decline observed in both patients with MCI and AD. In contrast to acetylcholinesterase inhibitors and N-methyl D-aspartate receptor antagonists, aducanumab and lithium may be disease-modifying drugs. Therefore, we focused on aducanumab and lithium and compared the effects of these drugs on the cognitive decline in MCI and AD patients using a network meta-analysis.

Methods: PubMed, the Cochrane Library, CINHAL, and ClinicalTrials.gov were searched for randomized controlled trials testing lithium or aducanumab for the treatment of cognitive decline in patients with MCI or AD, up to January 31, 2022. A frequentist fixed-effect network meta-analysis was performed to estimate direct and indirect effects. The primary outcome was change scores in cognitive decline measured by Mini-Mental State Examination. This study has been registered with PROSPERO (number CRD42022304807).

Results: Network meta-analysis demonstrated that lithium was significantly more effective than aducanumab in the primary outcome.

https://pubmed.ncbi.nlm.nih.gov/

Im Jahr 2021 erteilte die US-amerikanische Arzneimittelbehörde FDA eine **beschleunigte Zulassung für Aducanumab** für Patienten mit leichter kognitiver Beeinträchtigung (MCI) und leichter Demenz aufgrund von Alzheimer (AD); allerdings sind die **Kosten für Aducanumab** mit **etwa 28.000 US-Dollar pro Person und Jahr sehr hoch**.

Lithium hingegen ist mit **40 US-Dollar pro Jahr wesentlich günstiger** und hat sich [...] bei der kognitiven Abnahme sowohl **bei Patienten mit MCI als auch mit AD als wirksam erwiesen**.

Die Netzwerk-Metaanalyse zeigte, dass **Lithium** beim primären Endpunkt [*cognitive decline by MMSE*] **signifikant wirksamer** war **als Aducanumab**.

Review > Ageing Res Rev. 2024 Feb:94:102203. doi: 10.1016/j.arr.2024.102203. Epub 2024 Jan 20.

Comparative efficacy, tolerability and acceptability of donanemab, lecanemab, aducanumab and lithium on cognitive function in mild cognitive impairment and Alzheimer's disease: A systematic review and network meta-analysis

Itsuki Terao [1], Wakako Kodama [2]

January 20, 2024

Conclusion: Although it is yet to be determined which is more effective between lithium or lecanemab or donanemab, lithium may be more effective than aducanumab. Aducanumab, lecanemab and donanemab do not appear to differ in their effectiveness on cognitive function. Low-dose lithium may be safer than aducanumab, lecanemab and donanemab.

PMID: 38253184 DOI: 10.1016/j.arr.2024.102203

Aducanumab, Lecanemab und Donanemab scheinen sich in ihrer Wirkung[slosigkeit] auf die kognitiven Funktionen nicht zu unterscheiden.

Niedrig dosiertes Lithium würde eine sicherere Alternative zu Aducanumab, Lecanemab und Donanemab darstellen.

https://pubmed.ncbi.nlm.nih.gov/

Meta-Analysis > J Alzheimers Dis. 2024;98(3):825-835. doi: 10.3233/JAD-230911.

Comparative Efficacy, Tolerability, and Acceptability of Donanemab, Lecanemab, Aducanumab, Melatonin, and Aerobic Exercise for a Short Time on Cognitive Function in Mild Cognitive Impairment and Mild Alzheimer's Disease: A Systematic Review and Network Meta-Analysis

Itsuki Terao [1], Wakako Kodama [2]

March 6, 2024

Conclusions: Melatonin may be a better potential disease-modifying treatment for cognitive decline in mild AD and MCI. Aerobic exercise for a short time might also be better than donanemab, lecanemab and aducanumab if continued, as it is well tolerated and more effective, although less valid due to heterogeneity. Another limitation is the small number of participants.

PMID: 38461503 DOI: 10.3233/JAD-230911

„Melatonin könnte eine bessere krankheitsmodifizierende Behandlung für kognitiven Verfall bei leichter AD und MCI sein.

Aerobes Training […] wird gut vertragen und ist [ebenfalls] wirksamer […].“

https://pubmed.ncbi.nlm.nih.gov/38461503/

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SCIENCE MEDICINES HEALTH

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Home > News > Meeting highlights from the Committee for Medicinal Products for Human Use (CHMP) 22-25 July 2024

Meeting highlights from the Committee for Medicinal Products for Human Use (CHMP) 22-25 July 2024

Share

26 July 2024

14 new medicines recommended for approval; another 11 medicines recommended for extension of therapeutic indications

News | Human | Medicines

Negative opinion for one medicine

The CHMP recommended not granting a marketing authorisation for **Leqembi** (lecanemab), a medicine intended for the treatment of Alzheimer's disease. The committee considered that the observed effect of Leqembi on delaying cognitive decline does not counterbalance the risk of serious side events associated with the medicine, in particular the frequent occurrence of amyloid-related imaging abnormalities (ARIA), involving swelling and potential bleedings in the brain of patients who received Leqembi.

Der CHMP empfahl, **Leqembi** (Lecanemab), ein Arzneimittel zur Behandlung der Alzheimer-Krankheit, **nicht zuzulassen**. Der Ausschuss kam zu dem Schluss, dass **die beobachtete Wirkung** von Leqembi **auf die Verzögerung des kognitiven Abbaus das Risiko schwerwiegender Nebenwirkungen** des Arzneimittels, **insbesondere das häufige Auftreten von [...] Schwellungen und möglichen Blutungen** im Gehirn von Patienten, die Leqembi

https://www.ema.europa.eu/en/news/meeting-highlights-committee-medicinal-products-human-use-

MAYO CLINIC

Care at Mayo Clinic | Health Library | For Medical Professionals | Research & Education at Mayo Clinic | Giving to Mayo Clinic

Drugs & Supplements

Lecanemab-irmb (intravenous route)

Drug information provided by: Merative, Micromedex®

Portions of this document last updated: April 01, 2025

More common

- Back pain
- Blurred or changes in vision
- Chest tightness
- Chills
- Confusion
- Diarrhea
- Dizziness
- Dizziness, faintness, or lightheadedness when getting up suddenly from a lying or sitting position
- Drowsiness
- Feeling shaky
- Fever
- Flushing
- General feeling of discomfort or illness
- Headache
- Joint pain
- Loss of appetite
- Muscle aches and pain
- Nausea and vomiting
- Nervousness
- Pale skin
- Pounding in the ears
- Runny nose
- Seizures
- Shivering
- Slow or fast heartbeat
- Sore throat
- Sweating
- Trouble breathing
- Trouble sleeping
- Unusual tiredness or weakness

tagesschau

Sendung verpasst?

April 15, 2025

Startseite ▸ Wissen ▸ Gesundheit ▸ EU-Kommission lässt neuartigen Alzheimer-Wirkstoff Lecanemab zu

Wirkstoff Lecanemab

EU-Kommission lässt neues Alzheimer-Medikament zu

Stand: 15.04.2025 17:19 Uhr

Anders als bisherige Therapien soll der Wirkstoff Lecanemab die Alzheimer-Krankheit verlangsamen. Als erstes Medikament dieser Art erhielt es nun die Zulassung der EU. Infrage kommt es allerdings nur für wenige Patienten.

Die Europäische Kommission hat erstmals eine Alzheimer-Therapie zugelassen, die auf zugrundeliegende Krankheitsprozesse abzielt. Der Antikörper Lecanemab sei für eine Behandlung im frühen Stadium gedacht und damit das erste Medikament dieser Art, das in der EU zugelassen werde, teilte die Kommission mit.

?

THE LANCET *Regional Health* Europe

June 29, 2023

The affordability of lecanemab, an amyloid-targeting therapy for Alzheimer's disease: an EADC-EC viewpoint

Linus Jönsson [a] · Anders Wimo [a] · Ron Handels [a,b] · Gunilla Johansson [a] · Mercè Boada [c] · Sebastiaan Engelborghs [d] · et al. Show more

Affiliations & Notes · Article Info

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Show Outline

Summary

Lecanemab, an anti-amyloid antibody with effects on biomarker and clinical endpoints in early Alzheimer's Disease (AD), was granted accelerated approval by the FDA in 2023 and regulatory review in Europe is ongoing. We estimate the population potentially eligible for treatment with lecanemab in the 27 EU countries to 5.4 million individuals. Treatment costs would exceed 133 billion EUR per year if the drug is priced similarly as in the United States, amounting to over half of the total pharmaceutical expenditures in the EU. This pricing would be unsustainable; the ability to pay for high-priced therapies varies substantially across countries. Pricing similarly to what has been announced for the United States may place the drug out of reach for patients in some European countries. Disparities in access to novel amyloid-targeting agents may further deepen the inequalities across Europe in health outcomes. As representatives of the European Alzheimer's Disease Consortium Executive Committee, we call for pricing policies that allow eligible patients across Europe to access important innovations, but also continued investments in research and development. Infrastructure to follow up the usage of new therapies in routine care and new payment models may be needed to address affordability and inequalities in patient access.

Die Behandlungskosten würden 133 Milliarden Euro pro Jahr übersteigen, wenn das Medikament zu einem ähnlichen Preis wie in den Vereinigten Staaten angeboten würde, was mehr als der Hälfte der gesamten Arznei-

JOURNAL ARTICLE CORRECTED PROOF

A potential association between COVID–19 vaccination and development of Alzheimer's disease Get access ›

Jee Hoon Roh ✉, Inha Jung, Yunsun Suh, Min-Ho Kim

QJM AN INTERNATIONAL JOURNAL OF MEDICINE

RESEARCH ARTICLE | March 27, 2023 | Check for updates

Accelerated Brain Volume Loss Caused by Anti–β-Amyloid Drugs

May 16, 2023

A Systematic Review and Meta-analysis

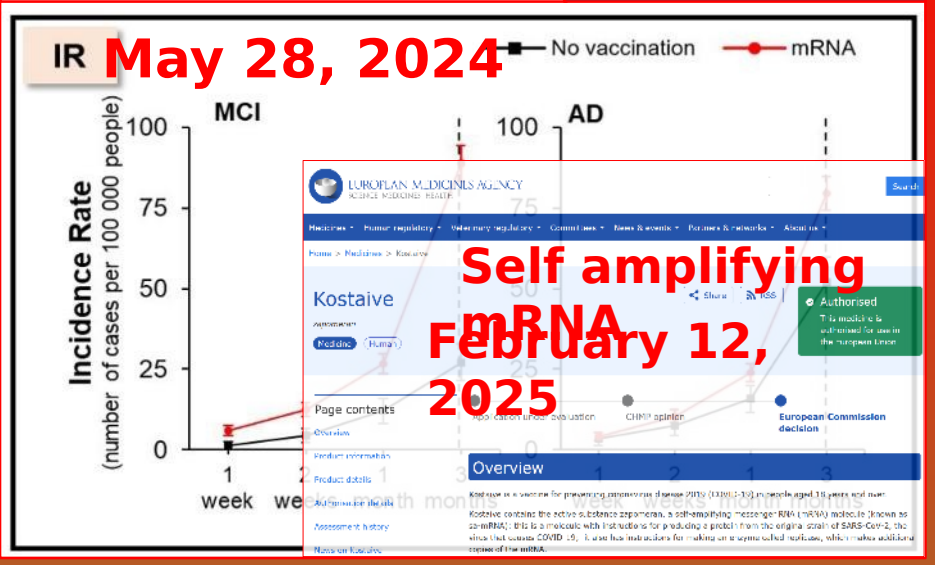
VIEW EDITORIAL

Francesca Alves, BBMED(Hons), PhD, Pawel Kalinowski, BBSc(Hons), MBiostat, PhD, and Scott Ayton, PhD AUTHORS INFO & AFFILIATIONS

May 16, 2023 issue • 100 (20) e2114-e2124 • https://doi.org/10.1212/WNL.0000000000207156

~~„Lithium healthy and effective alternative against MCI and AD.“~~

IR May 28, 2024



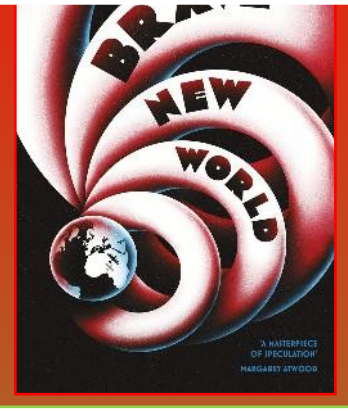
Self amplifying mRNA

February 12, 2025

“"Soma", a drug to cure any sort of unhappiness within society, causes "galloping senility"“

Aβ-vaccination

Spike mRNA injection



~~Lithium and Vit D: highly effective and protective against cytokine storm (COVID-19, UTAD (2016): etc.)~~

Acceleration of dementia: 2021 versus 2018: above age 65: +31.1%; below age 65: 25x!

Lithium deficiency

Alzheimer‘s risk

Fraiha-Pegado et al. International Journal of Bipolar Disorders (2024) 12:32 https://doi.org/10.1186/s40345-024-00348-5

International Journal of Bipolar Disorders

August 30, 2024

REVIEW Open Access

Trace lithium levels in drinking water and risk of dementia:

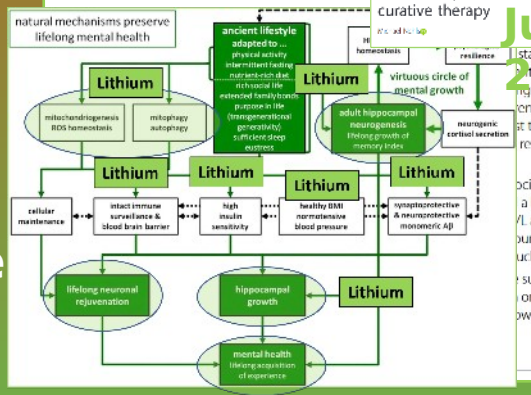
Julia Fraiha-Pegado[1], Vanessa J. Rodrigues de Pau

Journal of Molecular Psychiatry

REVIEW Open Access

Unified theory of Alzheimer's disease (UTAD): implications for prevention and curative therapy

July 15, 2016



A healthy lifestyle leads to an AD risk close to ze

https://www.alzheimer-bayern.de/images/downloads/demenz/8_Zahlen/infoblatt1_haeufigkeit_demenzerkrankungen_dalzg.pdf

Review > J Am Coll Nutr. 2002 Feb;21(1):14-21. doi: 10.1080/07315724.2002.10719188.

Lithium: occurrence, dietary intakes, nutritional essentiality

Gerhard N Schrauzer [1]

Affiliations + expand

PMID: 11838882 DOI: 10.1080/07315724.2002.10719188

February, 2002

Abstract

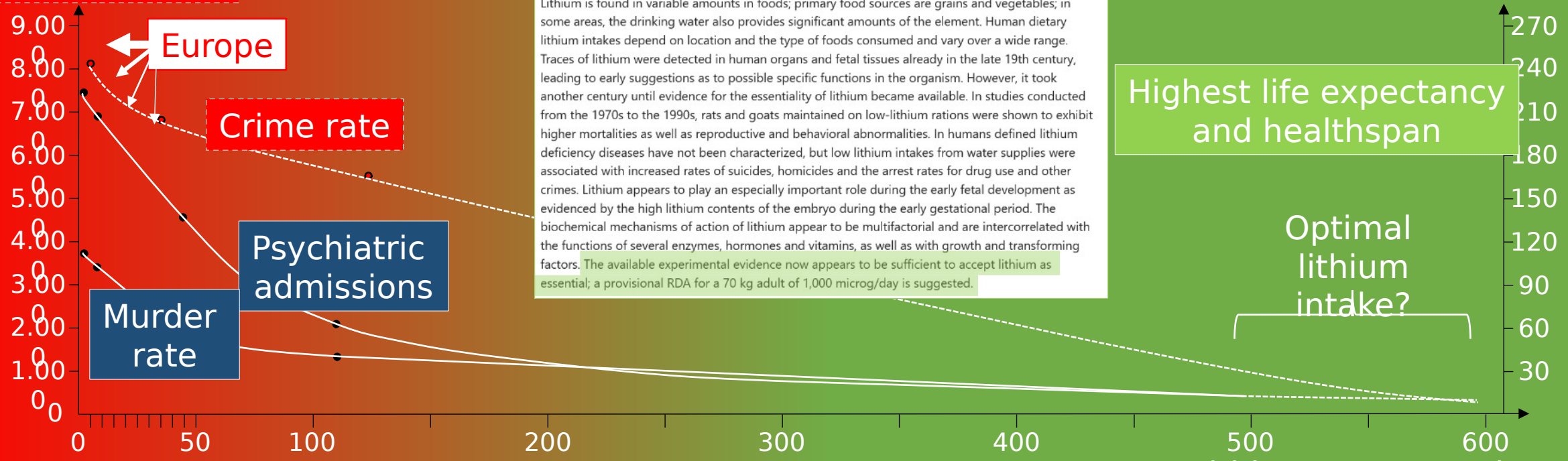
Lithium is found in variable amounts in foods; primary food sources are grains and vegetables; in some areas, the drinking water also provides significant amounts of the element. Human dietary lithium intakes depend on location and the type of foods consumed and vary over a wide range. Traces of lithium were detected in human organs and fetal tissues already in the late 19th century, leading to early suggestions as to possible specific functions in the organism. However, it took another century until evidence for the essentiality of lithium became available. In studies conducted from the 1970s to the 1990s, rats and goats maintained on low-lithium rations were shown to exhibit higher mortalities as well as reproductive and behavioral abnormalities. In humans defined lithium deficiency diseases have not been characterized, but low lithium intakes from water supplies were associated with increased rates of suicides, homicides and the arrest rates for drug use and other crimes. Lithium appears to play an especially important role during the early fetal development as evidenced by the high lithium contents of the embryo during the early gestational period. The biochemical mechanisms of action of lithium appear to be multifactorial and are intercorrelated with the functions of several enzymes, hormones and vitamins, as well as with growth and transforming factors. The available experimental evidence now appears to be sufficient to accept lithium as essential; a provisional RDA for a 70 kg adult of 1,000 microg/day is suggested.

Crime rate
per 100,000 inhabitants over 10 years

Psychiatric admissions and murder rate
per 100,000 inhabitants over 2 years

Highest life expectancy and healthspan

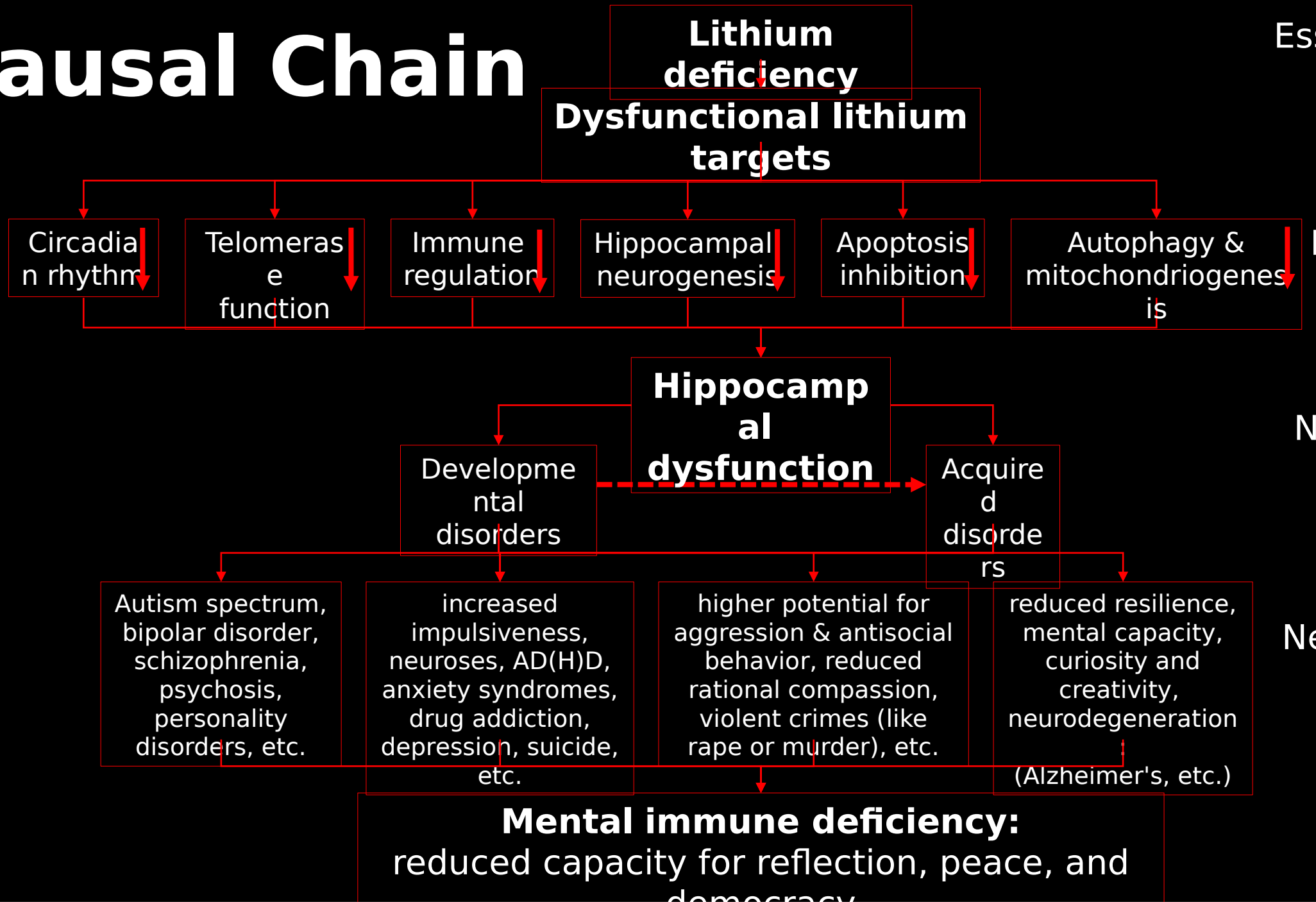
Optimal lithium intake?



„Die verfügbaren experimentellen Belege scheinen nun auszureichen,
um Lithium als essenziell anzuerkennen.
Für einen 70 kg schweren Erwachsenen wird eine vorläufige empfohlene Tagesdosis von 1.000 Mikrogramm pro Tag vorgeschlagen.“

https://jamanet

Causal Chain



Essential element

↓

Biochemical functions

↓

Physiological functions

↓

Neurobiological functions

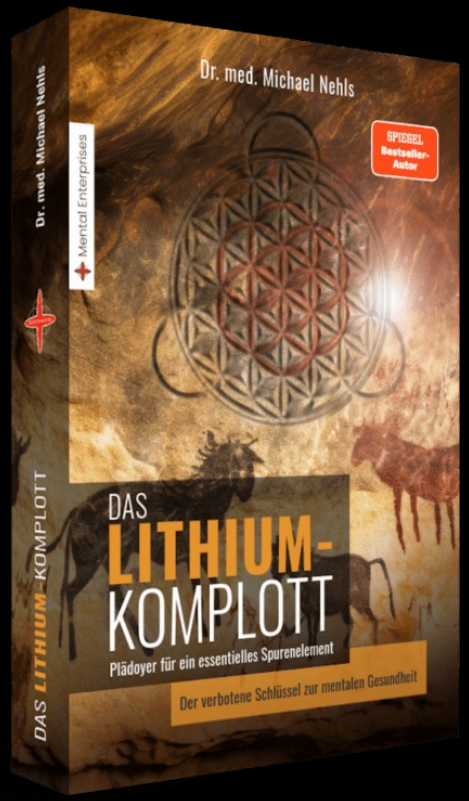
↓

Neuropsychiatric functions

↓

Social implications

Lithium is Essential



Argument 1: Lithium deficiency compromises both the mental and physical immune systems, causing many severe health problems.

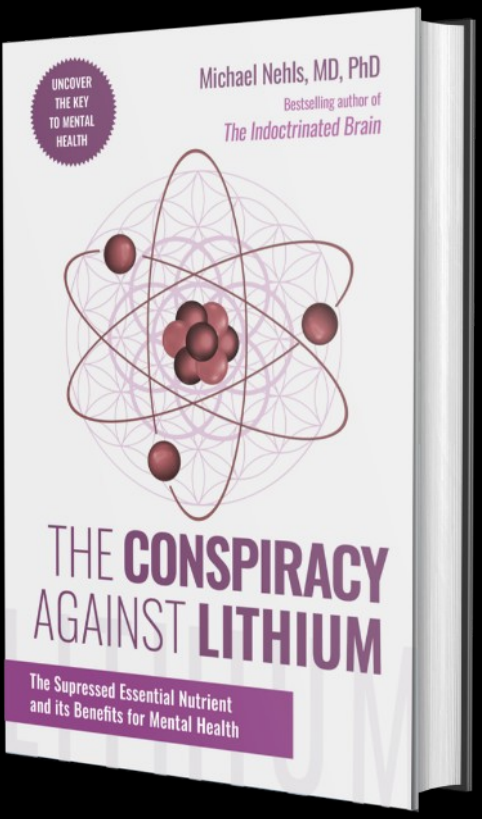
Argument 2: An established causal chain explains how lithium deficiency leads to clinical consequences via the dysregulation of lithium-dependent cellular information processors.

Argument 3: Lithium distribution is selectively regulated, typical for an essential trace element.

Argument 4: The regulation of lithium targets is highly conserved throughout evolution, from LUCA to humans (e.g., IMPase).

Argument 5: A severe lithium deficiency shortens the lifespan of animals and humans. An absolute deficiency is incompatible with life.

Argument 6: Correcting a lithium deficiency has been shown to extend the lifespan of several species. Higher lithium



1996

Trace elements in human nutrition and health

„Lithium kann bei Versuchstieren essentielle Funktionen haben, **aber es ist nicht bekannt, ob der Mensch einen Bedarf hat.**“

World Health Organization
Geneva
1996

„Epidemiologische Studien in den USA haben einen inversen Zusammenhang zwischen Lithium im Trinkwasser und der Sterblichkeit, insbesondere aufgrund von Herzerkrankungen und der Einweisungsrate in psychiatrische Kliniken gezeigt.“

generations on severely lithium-deficient rations, but the survival of the litters and reproductive efficiency were significantly reduced. Tissue lithium concentrations were found to reflect dietary lithium supply, except in some endocrine and exocrine glands and areas of the brain, in which near-normal concentrations were maintained even after prolonged depletion (*8*).

Epidemiological studies in the USA have shown negative correlations between lithium in drinking-water and mortality, especially from heart disease (*9*), and admission rates to mental hospitals (*10*).

In summary lithium at high, near toxic doses effectively controls the symptoms of manic-depressive disorders. Toxicity from dietary lithium is unknown, the intake from dietary sources being approximately 100 μg/day or less and, typically, less than 0.1% of the therapeutic or potentially toxic doses. Lithium may have essential functions in experimental animals but it is not known whether there is a human requirement.

https://www.who.int/publications/i/item/

Trace elements in human nutrition and health

„Lithium kann bei Versuchstieren essentielle Funktionen haben,
aber es ist nicht bekannt, ob der Mensch einen Bedarf hat.“

World Health Organization
Geneva
1996

Essential trace elements	Trace elements that are probably essential	Potentially toxic elements, some possibly with essential functions
Chromium	Boron	Fluorine
Iron	Manganese	Lead
Iodine	Nickel	Cadmium
Cobalt	Silicon	Mercury
Copper	Vanadium	Arsenic
Molybdenum		Aluminum
Selenium		Lithium
Zinc		Tin

https://www.who.int/publications/i/item/

Wissenschaftliche Dienste — Deutscher Bundestag

Dokumentation

November 25, 2022

Aluminiumhaltige Lebensmittel, Lebensmittelzusatzstoffe, Kosmetika, Lebensmittelkontaktmaterialien und Spielzeuge

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https://www.bundestag.de/resource/blob/928354/6a673927f71e5e93755e0a5987b42d23/

1949

THE MEDICAL JOURNAL OF AUSTRALIA

VOL. II.—36TH YEAR. SYDNEY, SATURDAY, SEPTEMBER 3, 1949. No. 10.

LITHIUM SALTS IN THE TREATMENT OF PSYCHOTIC EXCITEMENT.

JOHN F. J. CADE, M.D.,
Medical Officer, Victorian Department of Mental Hygiene.

Discussion.

There is no doubt that in mania patients' improvement has closely paralleled treatment and that this criterion has been fulfilled in the chronic and subacute cases just as closely as in the cases of more recent onset. The quietening effect on restless [illegible] additional strong evidence of the [illegible] especially as such restlessness [illegible] treatment.

Lithium salts have no appa[illegible] result is purely sedative. The eff[illegible] psychotic excitement—that is, tr[illegible] specific that it inevitably leads [illegible] possible ætiological significance [illegible] body of lithium ions in the genesis of this disorder.

Lithium may well be an essential trace element. It is widely distributed, has been detected in sea-water and in many spring and river waters, in the ash of many plants, and in animal ash.

Pre-frontal leucotomy has been performed lately on restless and psychopathic mental defectives (Mackay, 1948; Engler, 1948) in an attempt to control their restless impulses and ungovernable tempers. It is likely that lithium medication would be effective in such cases and would be much preferred to leucotomy.

guinea-pigs, it appeared desirable to ascertain whether uric acid enhanced this toxicity. The great difficulty was the insolubility of uric acid in water, so the most soluble urate was chosen—the lithium salt. When an aqueous solution of 8% urea, saturated with lithium urate, was injected, the toxicity was far less than was expected. It looked as if the lithium ion might have been exerting a protective effect. To determine this, more observations were made, lithium carbonate being used instead of lithium urate. An 8% aqueous solution of urea kills five out of ten guinea-pigs when injected intraperitoneally in doses of 1·25 millilitres per ounce of body weight. When 0·5% lithium carbonate in an 8% urea solution was injected in the same dosage, all ten animals survived; and this argued a strong protective function for the lithium ion against the convulsant mode of death caused by toxic doses of urea.

supposed efficacy was a real efficacy and directly proportional to the lithium content of the waters.

In the treatment of such a self-limiting disorder as mania, the therapeutic innovator must be more than ordinarily on his guard. Whether this or that treatment is of any value must be carefully assessed from as many angles as possible. With an episodic disorder of this type, the efficacy of a particular treatment may be judged by one or more of the following criteria. The more criteria that are satisfied, the more sure are we that it is a treatment of real and not suppositious value.

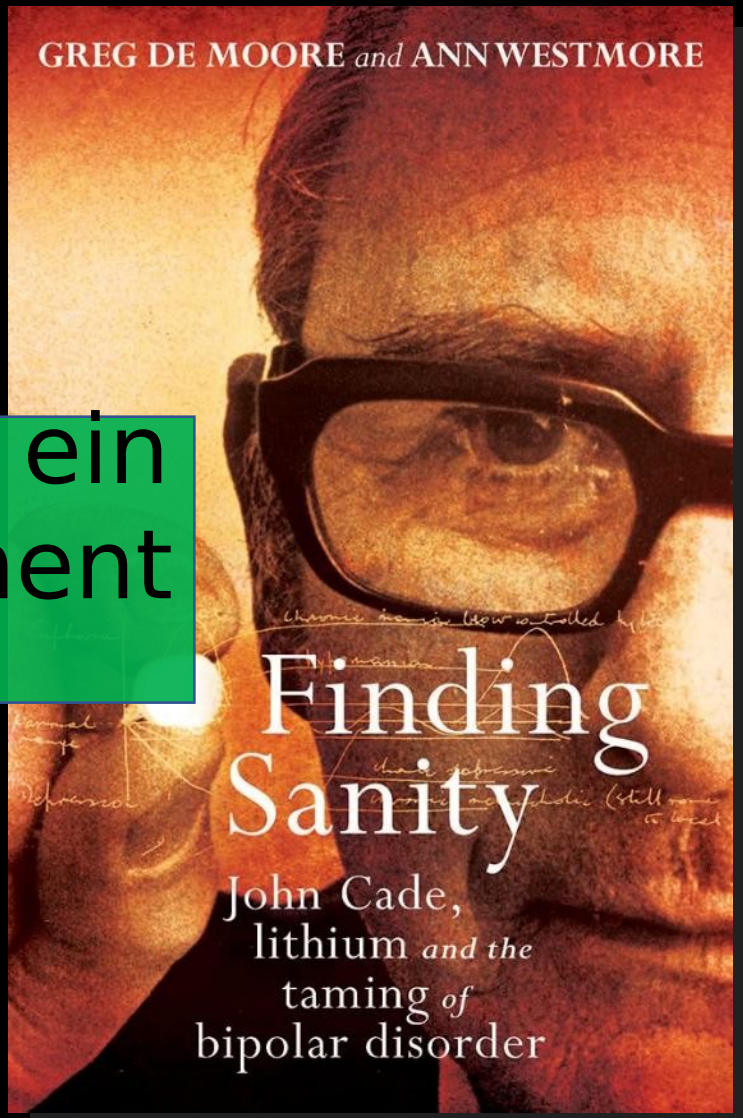
1. Improvement must proceed *pari passu* with treatment.
2. Chronic cases are of special value in assessment because in them spontaneous remission is far less likely to occur in a specified short period than in the recent cases.
3. Supporting evidence may be forthcoming from the treatment of non-manic psychotic excitement.
4. The ideal is, of course, the method of controlled observation of a sufficient number of treated and untreated patients. The disadvantage of the ideal is that mania is not so common a psychotic disorder as might be thought and it would take any one observer even in a large mental hospital probably some years to accumulate a large enough series to be statistically significant. But although the first three criteria may be insufficient for formal proof, they are capable of giving strong circumstantial evidence for or against efficacy.

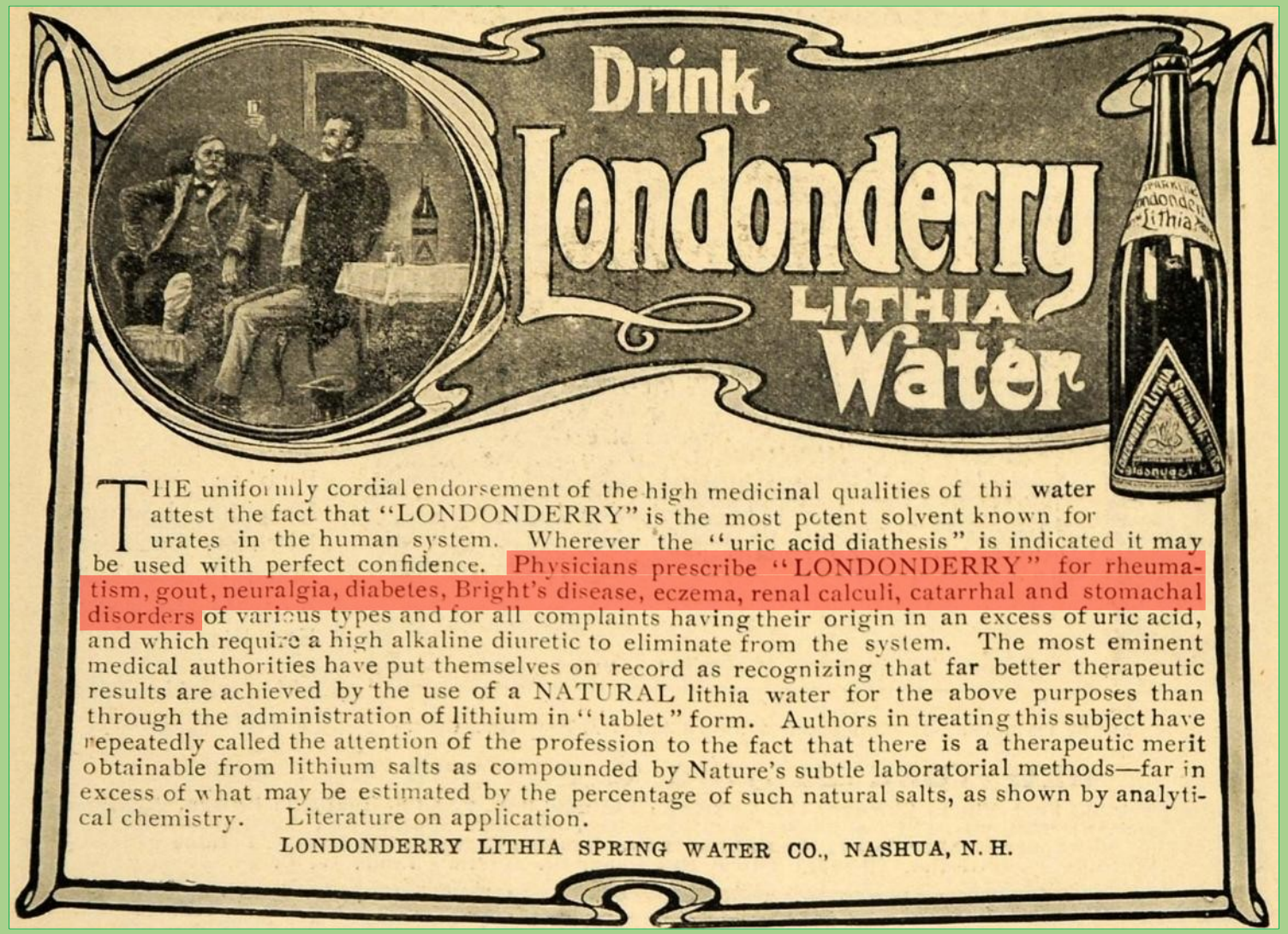
So far ten manic patients have been treated, of whom three suffered from chronic and the remainder from

518

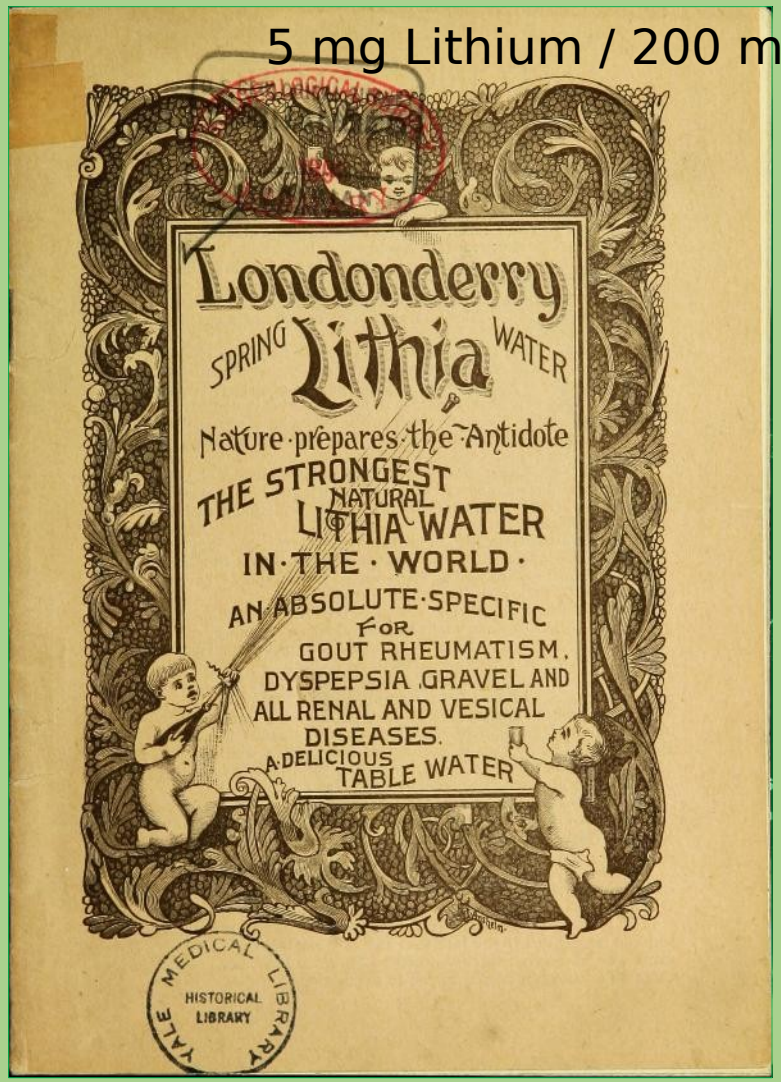
Bulletin of the World Health Organization, 2000, 78 (4)

„Lithium kann durchaus ein essentielles Spurenelement sein.“

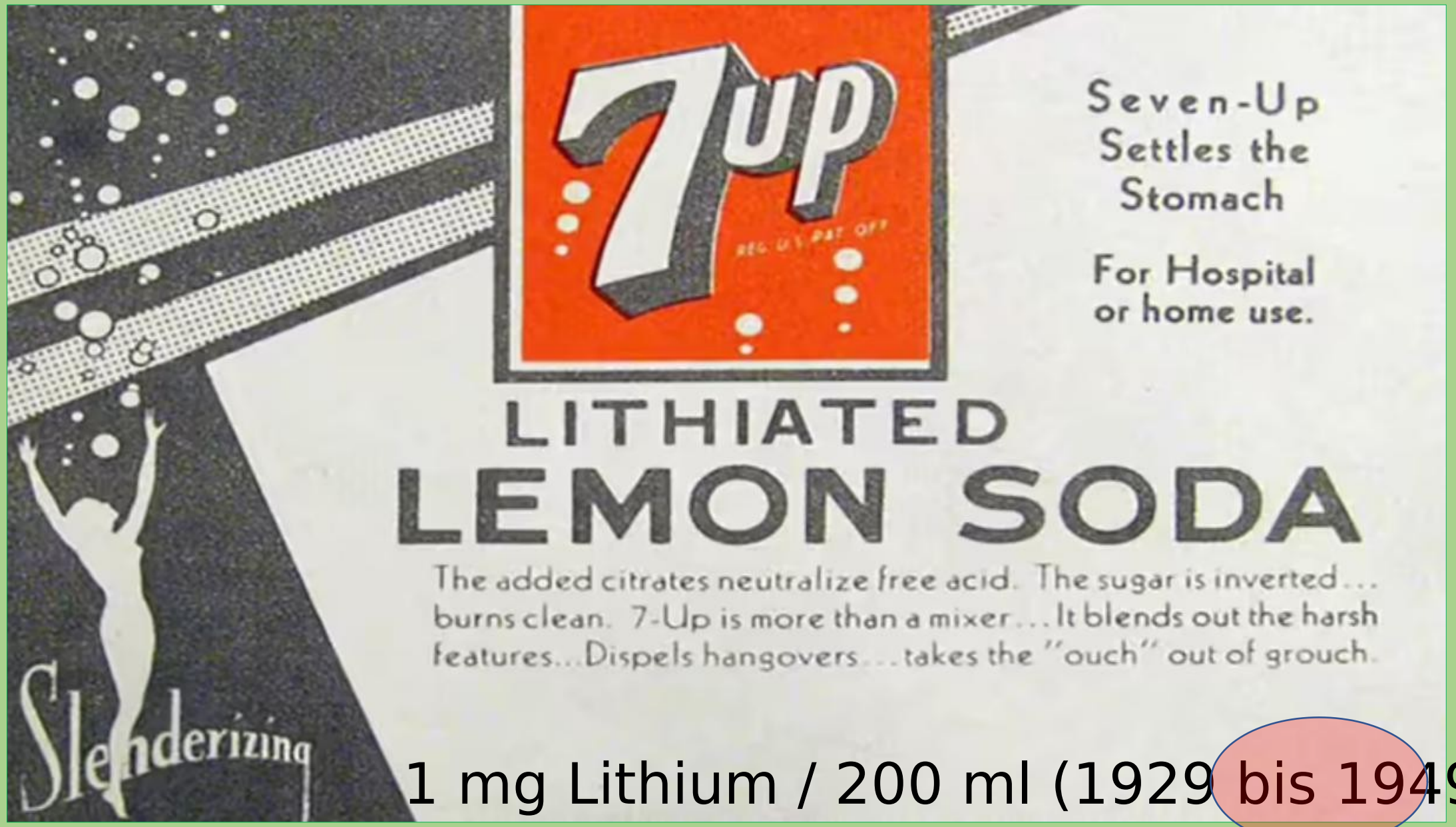




5 mg Lithium / 200 ml



„Ärzte verschreiben Londonderry gegen Rheumatismus, Gicht, Neuralgie [chronische Nervenschmerzen], Diabetes, Bright'sche Krankheit [chronische Nierenentzündung], Ekzeme [Hautausschläge], Nierensteine, Katarrh [Erkältungskrankheit] und verschiedene Magenbeschwerden […].“



1 mg Lithium / 200 ml (1929 bis 1949)

U.S.

Medicine: Case of trie Substitute Salt

TIME
FEBRUARY 28, 1949 12:00 AM GMT-5

28 . Februar 1949

TIME

People with high blood pressure, or some diseases of the heart and kidneys, are often forbidden to use salt. Last spring the Foster-Milburn Co. of Buffalo thought it had found something harmless that would give food a salty flavor. The new product, Westsal, contained lithium chloride (table salt is sodium chloride).

Early this month, doctors at a Manhattan hospital suspected that the substitute salt might have played a part in the death of a patient with heart disease. The Food & Drug Administration began experimenting, and found that heavy doses of lithium chloride killed laboratory animals. Then the FDA checked up on human patients taking the salt, found that they were suffering variously from drowsiness, weakness, loss of appetite, nausea, tremors, blurred vision, unconsciousness.

Whether the symptoms were due to the patients' diseases or to the lithium chloride, no one could positively say—at the time. But to play safe, the FDA ordered the Foster-Milburn Co. and two other manufacturers* of similar products to take them off the market.

Last week the case of the strange salt suddenly became more serious. A doctor in Ann Arbor, Mich, reported to Dr. Morris Fishbein, editor of the Journal of the American Medical Association, that a patient was critically ill, apparently from lithium chloride. Two days later three doctors from Cleveland's Crile Clinic sent in another report: two patients (one 70, the other 60) had died and five others were ill, apparently from the salt. Dr. Fishbein asked newspapers and radio stations to issue warnings. Planning to reclassify lithium chloride as a drug instead of as a special dietary food, FDA heard of the deaths and warned: "Stop using this dangerous poison at once."

*Foods Plus, Inc., Manhattan, makers of Foodsal; Lueth's Bakery, Kansas City, makers of Saltisal.

"Die FDA war gerade dabei, Lithiumchlorid als Medikament und nicht als Nahrungsergänzung zu reklassifizieren, als sie von den Todesfällen erfuhr und warnte:

Dieses gefährliche Gift darf ab sofort nicht mehr [als Nahrungsergänzung] verwendet werden."

The Journal of the American Medical Association

Published Under the Auspices of the Board of Trustees

VOL. 139, NO. 11 — CHICAGO, ILLINOIS — MARCH 12, 1949

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LITHIUM POISONING FROM THE USE OF SALT SUBSTITUTES

A. C. CORCORAN, M.D.
R. D. TAYLOR, M.D.

The purpo
lithium into
lithium chloride as a salt substitute for flavoring low sodium diets. We shall describe the syndrome as it was observed in 7 cases, in 2 of which the intoxication seems to have been a contributory cause of death. The salt substitute used by these patients was westsal,® which is a solution of lithium chloride with citric acid and a small amount of potassium iodide. That the cause of the intoxication was lithium ion, and not sodium depletion as such, seems evident from a study of these cases, in 1 of which the intoxication was induced as a clinical trial. Nevertheless, the data indicate that sodium depletion, incident to treatment with low sodium diets, increases the susceptibility to intoxication from orally ingested lithium salts.

A neurologic consultant noted, "I have never seen such striking muscular irritability in a cerebral lesion. Strychnine poisoning, tetanus and tetany should be considered." An electroencephalogram on August 9 showed a severe generalized slow dysrhythmia with frequencies of 4 to 6 per second and voltages up to 150 millivolts. A neurologic consultant suggested that such an electroencephalogram and clinical state might

49 volumes per cent on August 9. Serum potassium at the time was 3 milli
By August 1
by mouth; in succeedin
discharged in good cond
amnesia for the week of
the next ten days, and
westsal.® Again tremo
passed into coma and d
not obtained.

Summary.—In an
for congestive heart
of westsal® and of a
summer, a syndrom

„[…]die **Vergiftung** wurde **im Rahmen eines klinischen Versuchs** ausgelöst."

The lithium ban resulted from deaths that occurred when medical professionals instructed their patients to ingest lithium at doses over 1,000 times higher than the recommended daily allowance (RDA) of 1

710 LITHIUM CHLORIDE POISONING—STERN J. A. M. A. March 12, 1949

Clinical Notes, Suggestions and New Instruments

SEVERE LITHIUM CHLORIDE POISONING WITH COMPLETE RECOVERY

Report of Case

ROBERT L. STERN, M.D.
Beverly Hills, Calif.

This syndrome followed the use of a commercial salt substitute containing lithium chloride, citric acid and potassium iodide. The changes which occurred were profound and severe, yet transient, and the patient made a rapid and complete recovery. The signal symptoms and signs as they successively occurred over a period of a week included anorexia, rapid change in personality, lethargy, dysphagia and pain on swallowing, bradycardia, cutaneous hyperesthesia and hyperalgesia, muscular hyperirritability, profound general and multiple myoclonus and mental obfuscation.

15, Dr. Kutzmann, the urologic consultant, ordered carbachol in an attempt to initiate urination. After the third tablet, the patient had a reaction consisting of profuse perspiration and the appearance of cardiac extrasystoles for the only time during my observation of him. Blood pressure was 148 systolic and 70 diastolic. The administration of atropine shortly stopped the reaction, and there was no residual evidence at the end of two hours, the heart rate and tone again being normal. Bladder retention was not helped. His abnormally reddened tongue was considered a deficiency sign, and crude liver extract and vitamin B complex were given intramuscularly daily.

On January 16 and 17 he appeared depressed and a little feeble and his appetite was not good. His weight was 140 pounds (63.5 Kg.). He had lost perhaps 2 pounds (0.9 Kg.) for the diuresis following the administration of meralluride was slight. On January 17 his heart rate continued regular, but varied from 60 per minute down to 48. An electrocardiogram on this date revealed no changes from the previous tracings and no evidence of digitalis intoxication. Digitoxin had been discontinued on January 16 when his appetite started to decrease.

On January 18 (ninth day after return to Los Angeles) he had distinctly failed. He was markedly depressed and

E—HANLON ET AL. J. A. M. A. March 12, 1949

fourth day. Before dying, these animals became irritable and showed diffuse muscle tremors spontaneously and on stimulation.

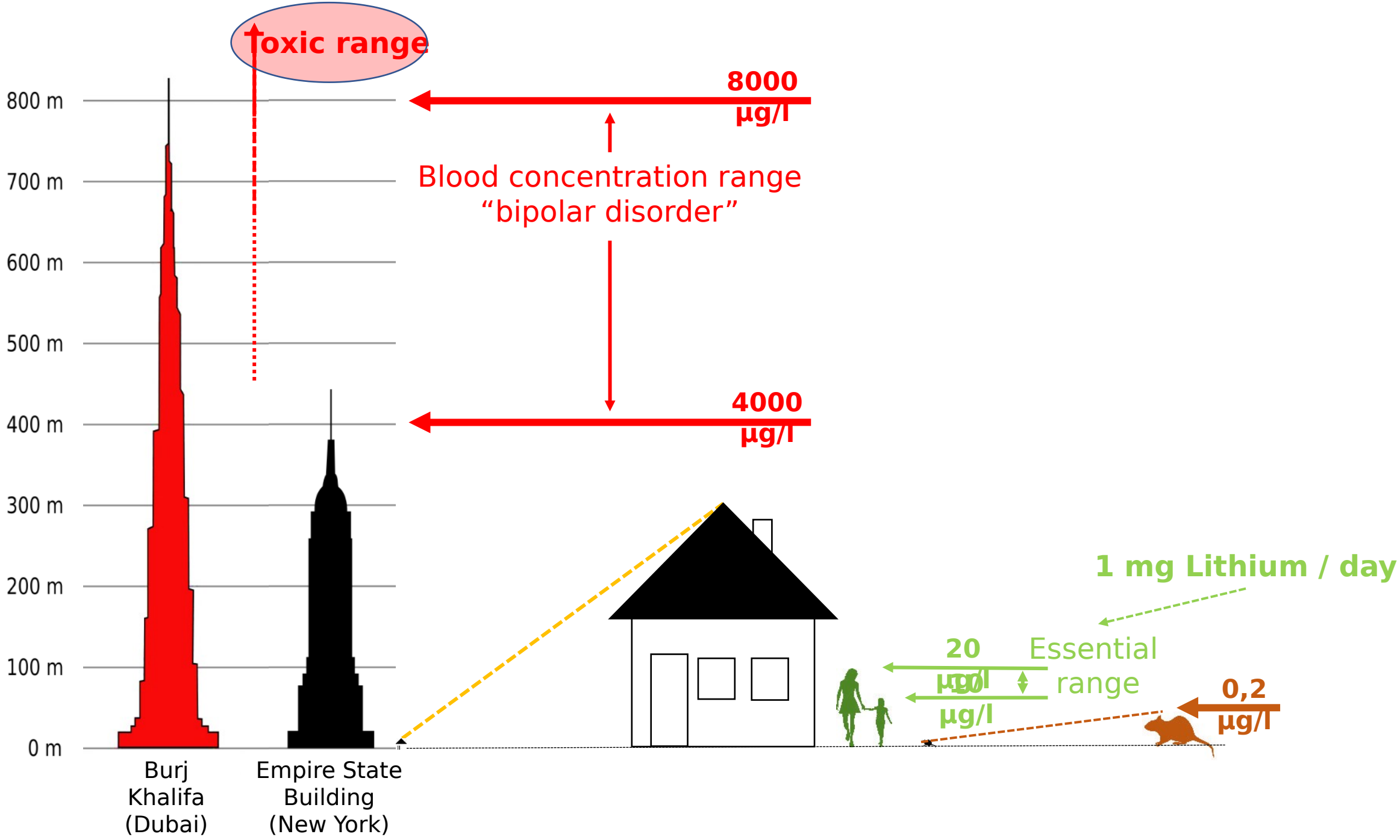
In contrast, rats given the sodium chloride supplements remained in good condition.

The data, which fit in well with the clinical studies reported, indicate toxicity of lithium chloride in rats given low sodium diets and a definite protection against lithium by the provision of supplementary sodium.

LITHIUM CHLORIDE AS A SUBSTITUTE FOR SODIUM CHLORIDE IN THE DIET

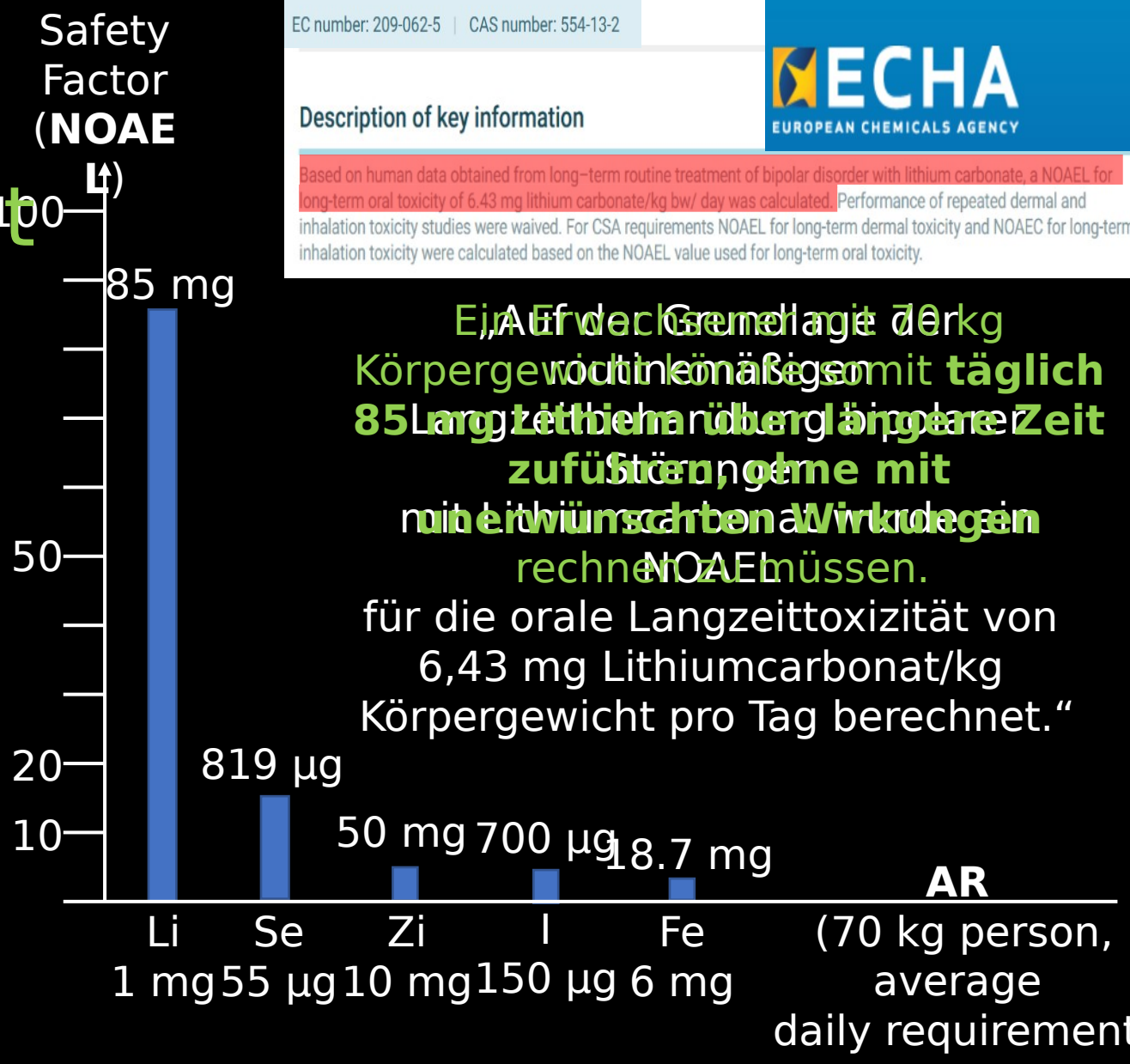
Observations on Its Toxicity

LAWRENCE W. HANLON, M.D.
MASON ROMAINE III, M.D.
FRANK J. GILROY, M.D.
New York
and
JOHN E. DEITRICK, M.D.
Chicago


Toxic range
800 m
700 m
600 m
500 m
400 m
300 m
200 m
100 m
0 m
8000 µg/l
Blood concentration range
“bipolar disorder”
4000 µg/l
1 mg Lithium / day
20 µg/l
Essential range
0,2 µg/l
Burj Khalifa (Dubai)
Empire State Building (New York)

thium is one of the safest essential trace elements

No **O**bserved **A**dverse **E**ffect **L**evel (**NOAEL**) / **A**verage **R**equirement (**AR**)



Lithium carbonate

EC number: 209-062-5 | CAS number: 554-13-2

Eine Agentur der Europäischen Union

ECHA
EUROPEAN CHEMICALS AGENCY

Description of key information

Based on human data obtained from long-term routine treatment of bipolar disorder with lithium carbonate, a NOAEL for long-term oral toxicity of 6.43 mg lithium carbonate/kg bw/ day was calculated. Performance of repeated dermal and inhalation toxicity studies were waived. For CSA requirements NOAEL for long-term dermal toxicity and NOAEC for long-term inhalation toxicity were calculated based on the NOAEL value used for long-term oral toxicity.

„Auf der Grundlage der vorliegenden Daten mit Lithiumcarbonat wurde ein NOAEL für die orale Langzeittoxizität von 6,43 mg Lithiumcarbonat/kg Körpergewicht pro Tag berechnet.“

Ein Erwachsener mit 70 kg Körpergewicht müsste somit **täglich 85 mg Lithium über längere Zeit zuführen, ohne mit unerwünschten Wirkungen** rechnen zu müssen.

enium: https://www.atsdr.cdc.gov/toxprofiles/tp92.pdf

https://ec.europa.eu/health/archive/ph_risk/committees/sct/documents/out197_en.pdf

e: https://echa.europa.eu/de/registration-dossier/-/registered-dossier/15294/7/1

Iron: https://cfpub.epa.gov/ncea/pprtv/documents/Ironandcompounds.pdf

AR: https://www.efsa.europa.eu/sites/default/files/2017_09_DRVs_summary_report.pdf

m: https://echa.europa.eu/bg/registration-dossier/-/registered-dossier/15034/7/6/1

Michael Nehls

The Medicine Of The Future

Health System Reform Program With Focus On Prevention And Causal Therapy: A Comprehensive Approach To Reforming The Physical, Mental And Social Health & Wellbeing Of Society

MICHAEL NEHLS, MD, PHD
JUN 10, 2025

June 10, 2025

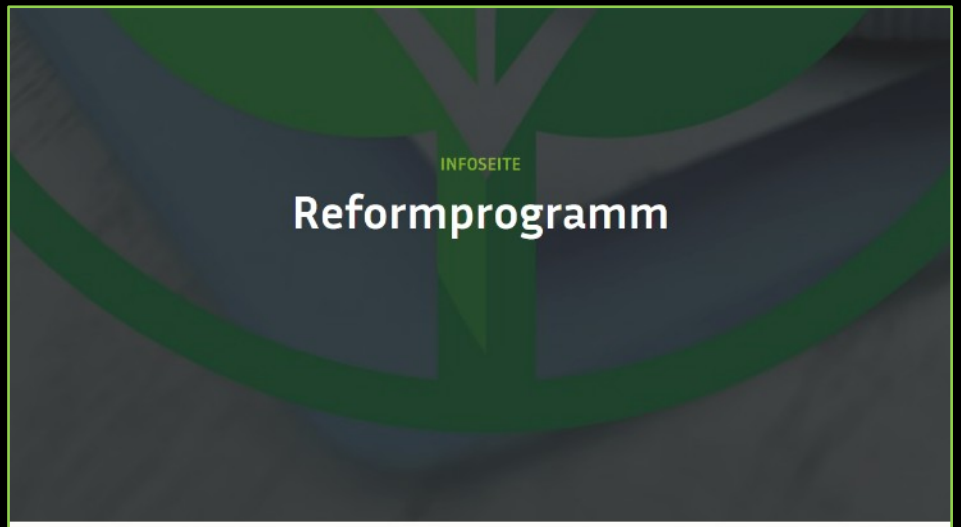
35 8 Share

Introduction

The history of medicine traces a significant evolution. The medical understanding that fundamental human needs—such as nutrition, sleep, physical activity, and social connection—are essential to health traces back to the teachings of Hippocrates of Kos. He emphasized the importance of living in harmony with nature. On this basis, two and a half thousand years ago, he developed a primarily preventive, systemic and deeply natural approach to medicine. Together with his students, he laid the foundations for nature-oriented medicine as an empirical science: health or illness were not random or fated developments, but had natural causes that – once understood – could also be influenced in natural ways. Man was thus not the plaything of divine whim but, like all life, part of nature and subject to its laws. With this revolutionary view, he undermined the almost absolute power of the priestly word in matters of illness and freed medicine from faith: it is not gods on Mount Olympus or elsewhere that cause illness and suffering, but a way of life that is not in harmony with natural needs. But the early 20th century saw the influence of Rockefeller medicine, which promoted exclusively a pharmaceutical-oriented approach. This led to the gradual exclusion and prohibition of natural medical practices such as osteopathy or herbal medicine, presenting them as less credible "alternative" medicine, as if the laws of nature did not apply to humans (see below, the Law of Minimum and Maximum required for healthy homeostasis). But there is no humane alternative to medical practice that respects natural human needs.

https://michaelnehls.substack.com/p/the-medicine-

Essential Lithium is an essential part of a **New Medical System** for infectious and chronic diseases – based on the **fundamental laws of life** (laws of the minimum, the



December 17, 202

Reformprogramm des Gesundheitssystems – Prävention und kausale Therapie

Ein notwendiger und umfassender Reformansatz für körperliche, psychische und soziale Gesundheit unserer Gesellschaft

– von PD Dr. Michael Nehls, 17. Dezember 2024

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1.3 Die Gesetze des Minimums und des Maximums als Fundamente einer präventiven Medizin
1.4 Achtung der persönlichen Autonomie
1.5 Bekämpfung von Unternehmenskorruption
1.6. Krankheitsprävention und Schutz vor pharmazeutischer Intoxikation
2. Konkrete Präventionsmaßnahmen und -strategien
2.1 Eigenverantwortung fördern und stärken
2.2 Reform der industriellen Einflussnahme auf die Politik, Forschung, Lehre und das öffentliche Leben
2.3 Reform des Krankenkassen- und medizinischen Vergütungssystems / Krankenkassen werden zu Gesundheitskassen
2.4 Reform medizinischer und allgemein heilberufliche Studiengänge bzw. Lehrpläne
2.5 Gesetzliche Maßnahmen zum Schutz der Bevölkerung
3. Abschlussbemerkungen

1. Allgemeine Grundsätze

1.1. Vorrang der artgerechten, krankheitsvorbeugenden und kausaltherapeutischen Lebensweise

Die moderne Medizin hat enorme Fortschritte gemacht. Insbesondere in der medikamentösen Akutbehandlung, aber auch in der chirurgischen Traumatologie. Die Lösung des enormen und ständig wachsenden Problems der sogenannten Zivilisationskrankheiten muss jedoch scheitern. Der Grund dafür liegt in einem grundlegenden, globalen Systemfehler: Multikausale Probleme sind nicht monokausal und schon gar nicht durch symptomatische Interventionen zu lösen – diese verschärfen das Problem sogar, weil sie es nur verschleiern und gleichzeitig aus Marktinteressen fördern (müssen). Hier kann nur ein multikausaler Ansatz, d. h. die Rückkehr zu einer artgerechten Lebensweise unter modernen Bedingungen und mit modernen Methoden sowie die Förderung einer gesundheitsbewussten Gesellschaft, in der die Befähigung zur Eigenverantwortung gefördert und unterstützt wird, die Lösung sein.

https://michael-nehls.de/infos/reformprogramm-gesundheitssystem/

Mental health

October 10, 2024

Latest progress report

European Commission

PAGE CONTENTS

- EU comprehensive approach to mental health
- Mental health situation in Europe
- Overview of actions on mental health
- Funding of mental health projects
- Governance
- Supporting Ukraine – mental health of displaced people and refugees
- Mental health and COVID-19
- Latest updates
- Documents

EU comprehensive approach to mental health

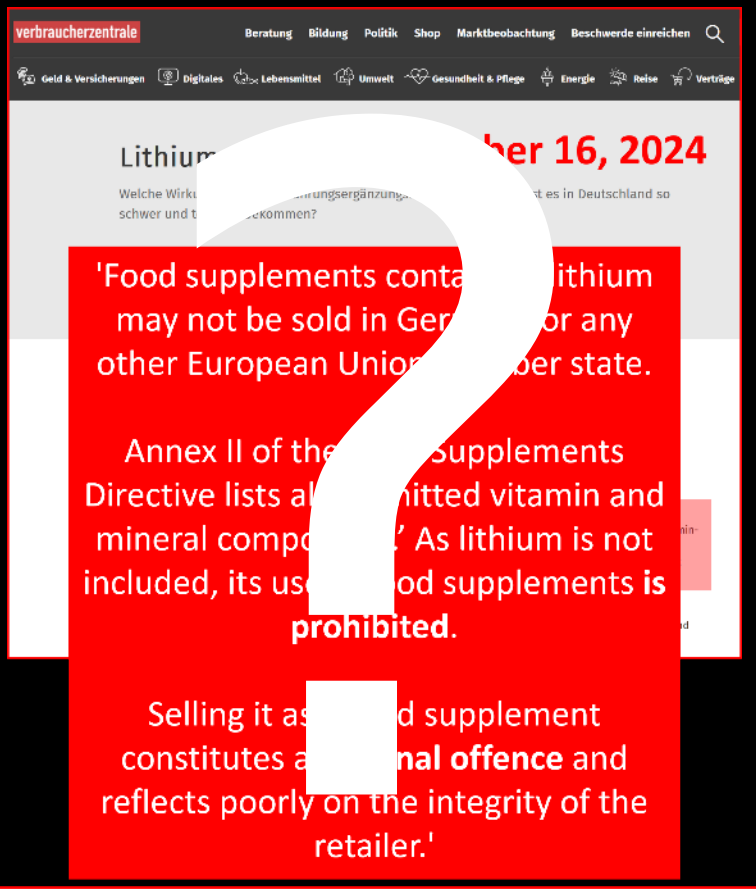
In her 2022 State of the Union speech, Commission President Ursula von der Leyen announced the Commission's intention to present "a new initiative on mental health" in 2023.

On 7 June 2023, the Commission adopted the Communication on a comprehensive approach to mental health, which will help Member States and stakeholders to take swift action to deal with mental health challenges.

The Communication is a starting point for a new approach. A **comprehensive, prevention-oriented and multi-stakeholder approach to mental health** has been developed after extensive consultation with Member States, stakeholders and citizens.

The new approach recognises that mental health strongly involves many policy areas, such as employment, education, research, digitalisation, urban planning, culture, environment and climate. This cross-sectoral approach aims to put physical health on par with mental health.

The initiative builds on existing policies, approaches and actions. The Communication's **20 flagships** – with financing opportunities worth **EUR 1.23 billion** – will directly and indirectly support Member States in achieving a comprehensive approach to mental health.



October 16, 2024

Already before the COVID-19 pandemic, 1 in 6 people in the EU suffered from mental health issues, at a cost of 4% of GDP.

The total costs of mental health problems are estimated at more than 4% of GDP (more than €600 billion) across the 27 EU countries and the United Kingdom (Health at a Glance Europe 2018 report).

https://www.verbraucherzentrale.de/faq/projekt-klartext-nem/lithiumorotat-40582

Financial Burden of Lithium Deficiency as Part of the “Old Medical System“ in Europe

estimated

1) Mental health € 600 billion / year
plus *lecanemab* (MCI) € 133 billion / year
2) Cancer € 200 billion / year
3) Cardiovascular Disease € 282 billion / year
4) COVID-19 (2020-2025) € 350 billion / year

€ 1615 billion / year

European Journal of Cancer 129 (2020) 41–49

Available online at www.sciencedirect.com
ScienceDirect
journal homepage: www.ejcancer.com

Original Research

April 2020

The cost of cancer in Europe 2018

Thomas Hofmarcher [a,*], Peter Lindgren [a,b], Nils Wilking [b], Bengt Jönsson [c]

[a] IHE - The Swedish Institute for Health Economics, Box 2127, SE-22002, Lund, Sweden
[b] Karolinska Institutet, Solnavägen 1, SE-17177, Solna, Sweden
[c] Stockholm School of Economics, Department of Economics, Box 6501, SE-11383, Stockholm, Sweden

Received 21 December 2019; received in revised form 16 January 2020; accepted 20 January 2020
Available online 28 February 2020

ESC European Society of Cardiology
European Heart Journal (2023) 44, 4752–4767
https://doi.org/10.1093/eurheartj/ehad583

FASTTRACK CLINICAL RESEARCH
Acute cardiovascular care

August 2023

Economic burden of cardiovascular diseases in the European Union: a population-based cost study

Ramon Luengo-Fernandez [1], Marjan Walli-Attaei[1], Alastair Gray [1], Aleksandra Torbica [2], Aldo P. Maggioni[3], Radu Huculeci [4], Firoozeh Bairami[4], Victor Aboyans [5], Adam D. Timmis[6], Panos Vardas [4,7], and Jose Leal [1]*

[1]Health Economics Research Centre, Nuffield Department of Population Health, University of Oxford, Old Road Campus, Oxford OX3 7LF, UK; [2]Centre for Research on Health and Social Care Management (CERGAS), Bocconi University, Milan, Italy; [3]ANMCO Research Center-Heart Care Foundation, Firenze, Italy; [4]European Society of Cardiology, European Heart Agency, Brussels, Belgium; [5]Department of Cardiology, Dupuytren University Hospital and EpiMaCT, Inserm1098RD270, Limoges University, Limoges, France; [6]William Harvey Research Institute, Queen Mary University London, London, UK; and [7]Biomedical Research Foundation Academy of Athens and Hygeia Hospitals Group, HHG, Athens, Greece

Received 27 July 2023; revised 15 August 2023; accepted 24 August 2023; online publish-ahead-of-print 26 August 2023

BRIEFING

EPRS | European Parliamentary Research Service
Author: Laurence Amand-Eeckhout
Members' Research Service
PE 751.416 – July 2023

European Parliament

July 2023

Mental health in the EU

Mental health disorders weigh heavily on societies and economies. According to the Commission, based on OECD data, the **economic burden** of mental ill health can rise to up to 4 % of EU gross domestic product (GDP) annually, equivalent to over €600 billion per year, owing primarily to reduced productivity, healthcare costs, and social welfare expenditure. These direct costs do not include indirect costs (e.g. informal care provided by family members) or intangible costs (the emotional distress, pain and suffering experienced by those with mental health problems and those close to them).

EUROPEAN COURT OF AUDITORS / news

Auditors reveal lessons from weaknesses in the EU's €650 billion recovery pot

06/05/2025 | COVID-19

- EU recovery fund brought a new approach to EU spending decoupled from costs
- Auditors warn about its many weaknesses ahead of key EU budget decisions
- The RRF suffers from insufficient focus on performance, and weak control

May 2025

The EU's COVID recovery fund – the Recovery and Resilience Facility (RRF) – suffers from several weaknesses in terms of performance, accountability and transparency, the European Court of Auditors (ECA) observes in its review of the €650 billion crisis spending. Although the RRF has played a crucial role in the EU's post-pandemic recovery, information on results is scarce, and there is no information on actual costs. As a result, it is not clear what citizens actually get for their money. The auditors call on EU policy makers to draw lessons from this when mulling future budgets based on performance rather than costs.

Overview of the Commission's response

Find out how the von der Leyen Commission helped the EU overcome COVID-19, supporting vaccines rollout and protecting livelihoods, and prepares for health threats.

PAGE CONTENTS

About
Securing safe and effective vaccines for Europe and the world
Economic measures
Public health
Borders and mobility
Fighting disinformation
Documents

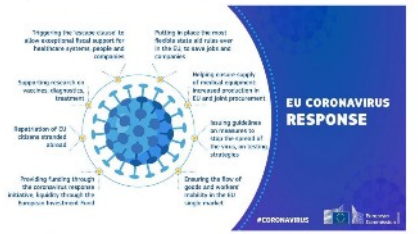
June 2025

About

The European Commission is working on all fronts to contain the spread of the coronavirus, support national health systems and counter the socio-economic impact of the pandemic by taking unprecedented measures at both national and EU level.

European Commission's coronavirus response team

Examples of how the Commission has helped to tackle the crisis:



The Non-Recognition of Lithium as an Essential Trace Element e Resulting Ban on Supplements is Contrary to Fundamental Human

Human dignity is inviolable. *However, it is violated when laws make it difficult to access essential substances such as lithium, when a health-threatening deficiency cannot be easily remedied with dietary supplements.*

Fundamental right to physical integrity. *Current legislation prohibits dietary supplements containing essential amounts of lithium although Lithium deficiency causes neuropsychiatric developmental disorders, among other issues, and has been proven to impair mental and physical health. Therefore, physical integrity is impaired.*

Tacitus (55–120 AD), Roman historian: "Formerly we suffered from crimes; now we suffer from laws."

Die Würde des Menschen ist unantastbar. Sie wird jedoch angetastet, wenn Gesetze den Zugang zu lebenswichtigen Substanzen wie Lithium erschweren und ein gesundheitsgefährdender Mangel nicht ohne Weiteres durch eine Nahrungsergänzung behoben werden kann.

Grundrecht auf körperliche Unversehrtheit. Die derzeitige Gesetzgebung verbietet Nahrungsergänzungsmittel, die essentielle Mengen an Lithium enthalten, obwohl Lithiummangel unter anderem neuropsychiatrische Entwicklungsstörungen verursacht und nachweislich die geistige und körperliche Gesundheit und damit die körperliche Unversehrtheit beeinträchtigt.

Tacitus (55–120 n. Chr.), römischer

The Non-Recognition of Lithium as an Essential Trace Element and the Resulting Ban on Supplements is Antidemocratic

Democracy depends on citizens, capable of reason, who in turn depend on a functioning mental immune system.

Demokratie ist auf mündige Bürger angewiesen, die wiederum auf ein funktionierendes mentales Immunsystem angewiesen sind.

Lithium deficiency weakens the mental immune system and hence a fundamental requirement for democratic thinking.

Lithiummangel schwächt das mentale Immunsystem und damit eine Grundvoraussetzung für demokratisches Denken.

A prescription requirement for this essential trace element is therefore incompatible with an EU policy that claims to defend and strengthen democracy.

Eine Verschreibungspflicht für dieses lebenswichtige Spurenelement ist daher unvereinbar mit einer EU-Politik, die behauptet, die Demokratie zu verteidigen und zu stärken.

Citizens with a functioning mental immune system are fully capable of deciding on their own what kind of

Bürger mit einem funktionierenden mentalen Immunsystem sind voll und ganz in der Lage, selbst zu entscheiden, welche

Only nature can determine what is essential for humans.

Therefore, based on scientific data and the dramatic health and political consequences of a chronic lithium deficiency, especially with regard to mental health, the following demands are made:

1) Recognition of lithium as an essential trace element

2) Inclusion in Annex II of the Food Supplements Directive, thereby repealing the absurd prescription requirement for essential amounts of lithium

3) Promotion of public education about the essentiality of lithium, including its inclusion in medical curricula

Nur die Natur kann bestimmen, was essentiell für den Menschen ist.

Basierend auf der wissenschaftlichen Datenlage und den dramatischen gesundheitlichen
und politischen Konsequenzen eines chronischen Lithiummangels, insbesondere in Bezug die mentale Gesundheit, werden folgende Forderungen gestellt:

1) Anerkennung von Lithium als essentielles Spurenelement

2) Aufnahme in Anhang II der Nahrungsergänzungsrichtlinie und damit Aufhebung der absurden Rezeptpflicht essentieller Mengen an Lithium

3) Förderung der Aufklärung der Bevölkerung über die Essentialität von Lithium bis hin zur Aufnahme in medizinische Lehrpläne

Today, I delivered an essential message here in the EU Parliament.

*This creates a favorable setting for everyone to approach their local politicians and **demand** dialogue with reference to this speech in the EU Parliament.*

Ich habe heute eine essentielle Botschaft hier im EU-Parlament öffentlich vorgetragen.

Es ist damit für jeden eine gute Voraussetzung geschaffen, auf seine lokalen Politiker zuzugehen, um den Dialog unter Verweis auf diesen Vortrag im EU-Parlament **einzufordern**.